RESISTANCE IS LESS OF A PROBLEM

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SENSITIVITY OF 100 STRAINS OF HEMOLYTIC STAPHYLOCOCCUS AUREUS TO CHLOROMYCETIN AND OTHER IMPORTANT ANTIBIOTIC AGENTS*

*This graph is adapted from Kempe, C. H.: *California Med.* 84:242, 1956. The single bar designated as "Antibiotics F" represents three widely used, chemically related agents grouped together by the investigator. Strains isolated January-June, 1954.

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is a potent therapeutic agent and, because certain blood dyscrasias have been associated with its administration, it should not be used indiscriminately or for minor infections. Furthermore, as with certain other drugs, adequate blood studies should be made when the patient requires prolonged or intermittent therapy.

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A REPORT ON A PROMISING CONCEPT IN ANTIMICROBIAL THERAPY: CONCURRENT ADMINISTRATION OF CHLOROMYCETIN AND GAMMA GLOBULIN

In treatment for infection, the physician is confronted with complex interactions between pathogen, antimicrobial agent and host. The pathogen represents the unselected factor, the therapeutic agent the component over which the physician exercises maximum control. But even with optimal antibiotic therapy, the eventual elimination of the infective agent and the resolution of pathologic changes depend upon efficient host response.[1,2]

Passive transfer of antibodies through gamma globulin provides a broad antibacterial spectrum because of origin in adults exposed to a variety of microorganisms. Employed as a protective element against some of the more common contagious diseases, gamma globulin permits more competent participation by the host in the fight against established infection.

Rationale for immuno-antibiotic therapy lies in simultaneous direct attack on the pathogen and re-enforced host resistance, which implies usefulness in treatment for acute fulminating, highly refractory, or prolonged infections.

EXPERIMENTAL STUDIES ENCOURAGING

In carefully controlled studies in mice, Fisher and his colleagues in Parke-Davis Research Laboratories, using pooled human gamma globulin and Chloromycetin (chloramphenicol, Parke-Davis) concurrently, demonstrated a high degree of therapeutic effectiveness in infected animals.[3] Five types of infection induced with species of Staphylococcus aureus, Streptococcus pyogenes, Proteus vulgaris and Pseudomonas aeruginosa responded to joint therapy with gamma globulin and Chloromycetin, each agent having shown at deliberately low doses in previous work little or no activity in these mouse infections when used separately. Fisher's experiences with hemolytic streptococci have been confirmed.[4]

Tests now in progress with pneumococci, salmonellae and additional strains of pseudomonas and proteus indicate that marked increases in survival rates may be anticipated in any infection where chloramphenicol has previously demonstrated therapeutic activity.[3] These observations suggest that immuno-antibiotic therapy can effect cures in a variety of refractory microbial diseases.

PROMISING IN EARLY CLINICAL TRIAL

Observations analogous to those of Fisher have been reported from the clinic.[5-7] More recently, the clinical use of gamma globulin in conjunction with antibiotics was undertaken by Waisbren[8] on the basis of Fisher's experimental work. His series of 46 patients with systemic and localized infections due to various strains of staphylococcus, pseudomonas, salmonella, proteus and to the pneumococcus had failed to respond to maximum effort with conventional therapeutic measures. Marked clinical improvement in six of these acutely ill patients shows clearly "...that in certain instances the addition of gamma globulin to antibiotic therapy may give a clinical result that could not have been obtained with the antibiotics used alone. In each of these cases, a long and extensive control period in which antibiotics were being vigorously administered had failed to produce a response but when gamma globulin was given with approximately the same dosages of antibiotic, rather marked improvements occurred."[8]

While the precise mechanism underlying the salutary effect of gamma globulin remains to be clarified, the existence of quantitative hypogammaglobulinemia was ruled out in patients in this series.[8]

A RATIONALE FOR IMMUNO-ANTIBIOTIC THERAPY

Although the relationship of susceptibility to infection and status of the host is well recognized, host resistance is an aspect of infectious disease still not understood in an era of extensive and of massive antibiotic therapy. Most antibiotics, in concentrations tolerated by living tissues, have bacteriostatic rather than bactericidal effect. In the clinic, bacteriostatic doses are most frequently given and host defense mechanisms are responsible for the eventually satisfactory clinical result.[4]

The problem of therapeutic failures despite vigorous courses of antibiotic therapy may be due to some disturbance in the immune process.[9] In addition, disproportionately high mortality rates in the extremes of life lend support to the impression of inadequate defense mechanisms, since these are underdeveloped and immature in the very young and may be impaired or depressed in the aged.[4]

Any discussion of immuno-antibiotic treatment must at present remain largely conjectural. From preliminary evidence, however, this approach to therapy appears worthy of consideration, especially in patients in whom adequate antibiotic therapy for active infectious processes has been disappointing. While the concept of enlisting the aid of the host in combating pathogenic microbes, thereby affording the physician control of two of the three principal interacting factors, is not new, enhancement of host resistance through use of gamma globulin in treatment for microbial disease is indeed a promising one.

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THE JOURNAL
of the
KANSAS MEDICAL SOCIETY

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Ownership: The Journal is a non-profit publication owned and published monthly by the Kansas Medical Society.

Subscription: A year's subscription to the Journal is included in membership in the Kansas Medical Society, with $2.00 of each member's dues apportioned to the Journal. Rates to others, except in foreign countries, $4.00 per year or 60c per copy.

Material: Scientific articles, editorials, and data of general interest are invited from all members. Articles are to be submitted on condition that they are contributed solely to this publication. A right is reserved to reject any material deemed unsatisfactory.

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Advertising: All advertising contracts, and all copy from advertisers under contract are subject to approval of the editorial board. Copy should be received by the 15th of the month immediately preceding the month of publication.

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Entered as second-class matter at the post office at Fulton, Missouri, June 19, 1953, under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on July 2, 1918. Office of Publication: 1201-05 Bluff Street, Fulton, Missouri.

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1. Proudfit, P. T., and Robinson, C. H.: Nutrition and Diet Therapy, ed. 11, New York, The Macmillan Company, 1955, pp. 314-320.
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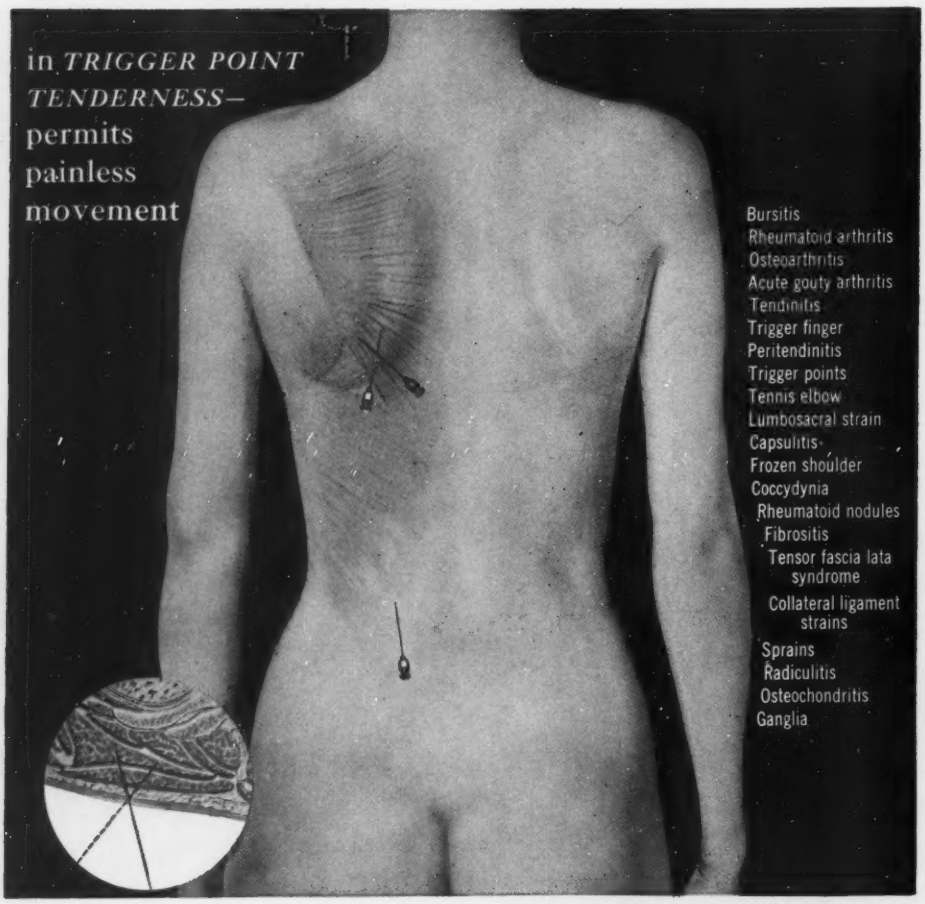

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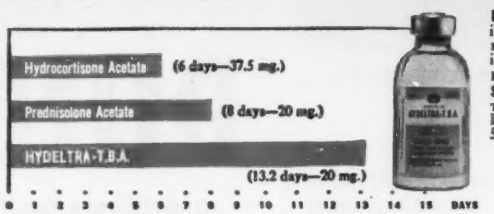
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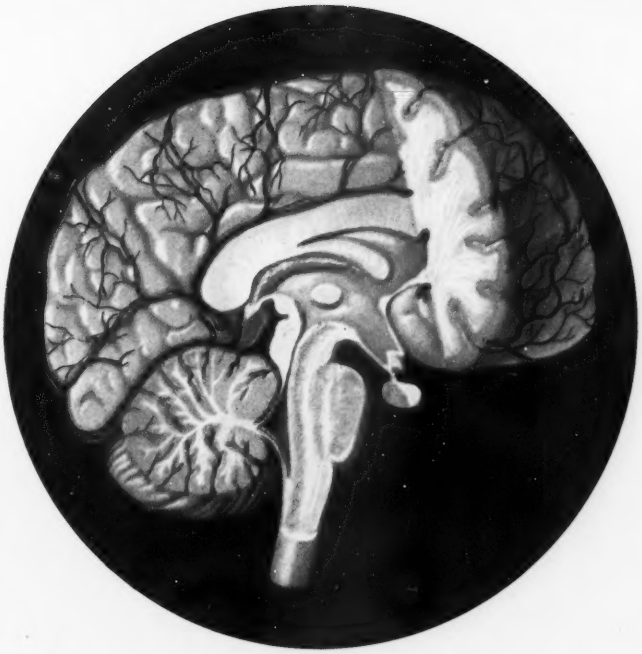

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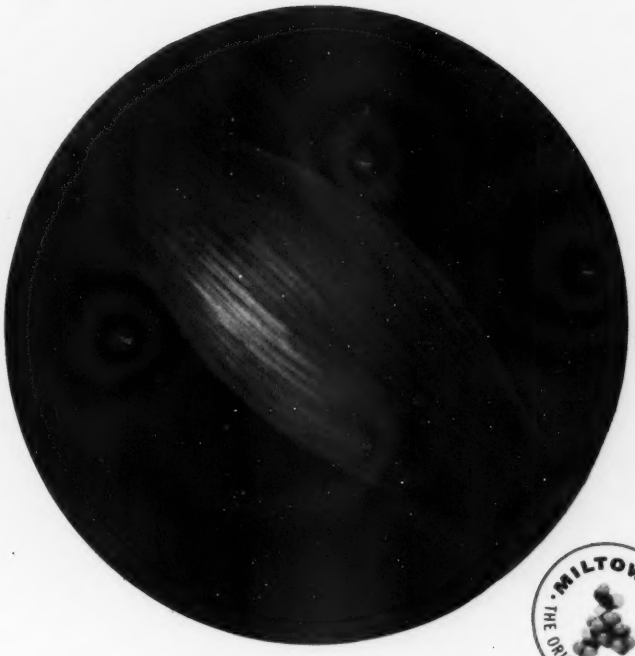

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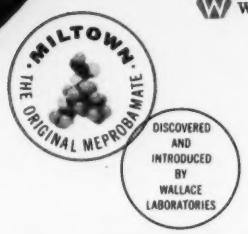

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Keyes, B. L.: Pennsylvania M. J. 60: 177, Feb. 1957.

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3	675		
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6	800		
7	825	100	45
8	850		
9	875		
10	900	95	43
11	950		
12	1000		
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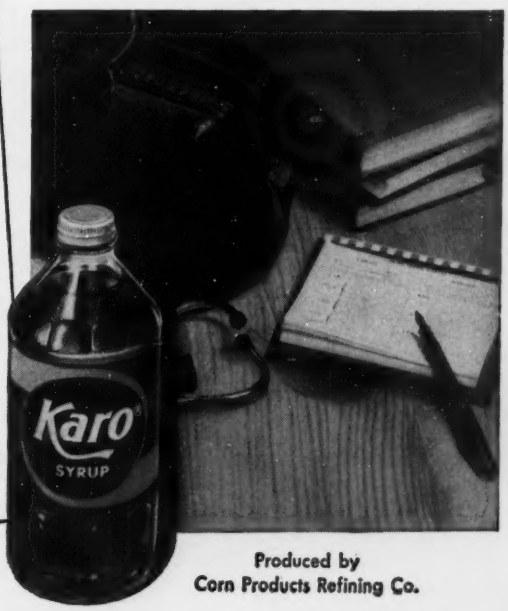

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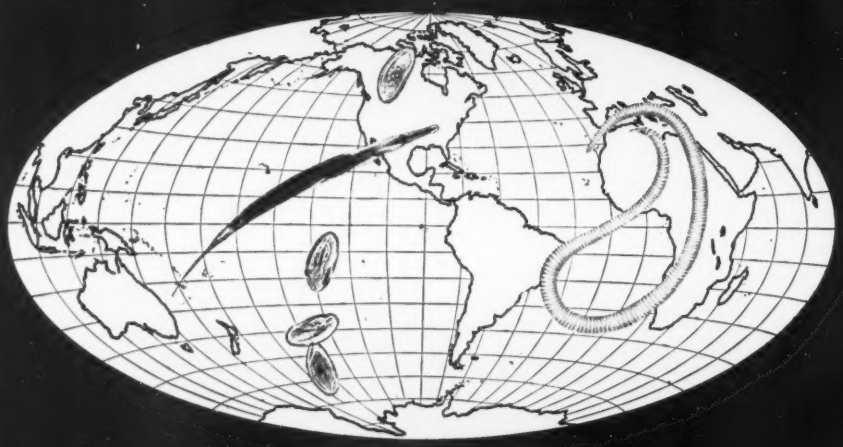

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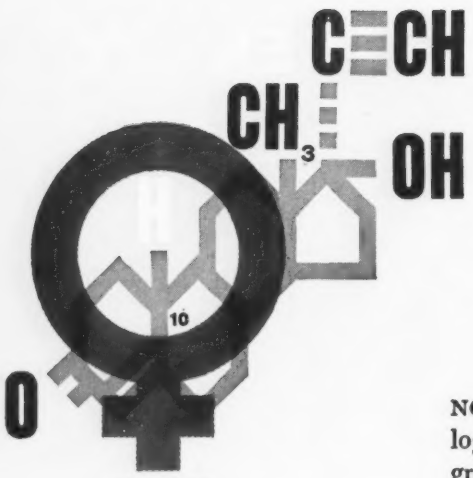

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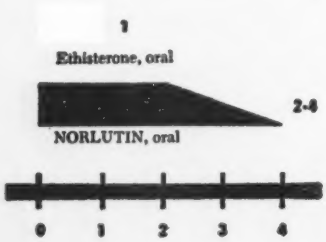

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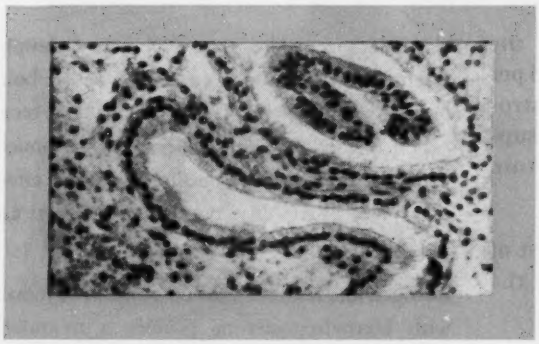

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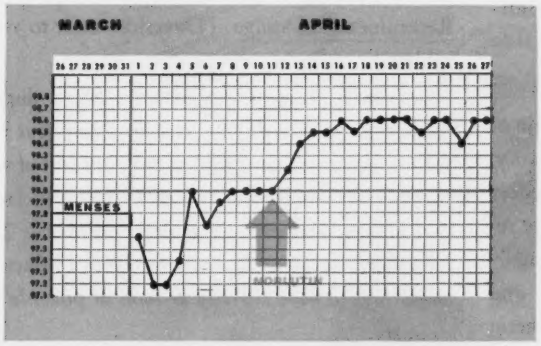

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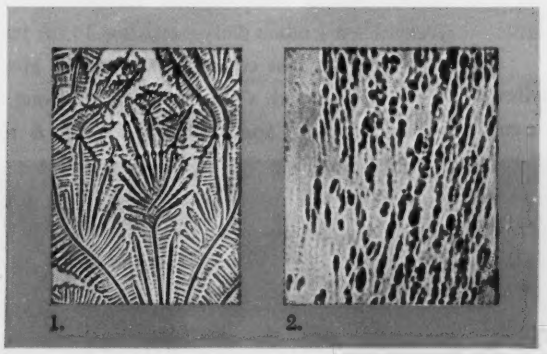

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Combined Estrogen-Androgen Therapy Proved 96% Effective in Preventing Postpartum Breast Engorgement[1]

Dual Steroid Approach also Successful in Osteoporosis

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Osteoporosis also ranks high on the list of present day medical problems because of the increasing older population.

In either condition, combined estrogen-androgen therapy produces a complementary metabolic response with little or no side effects.

In postpartum breast engorgement the rationale of therapy is explained as follows: During pregnancy, the high estrogen titer exerts an inhibitory effect on the anterior pituitary, thereby preventing the release of the lactogenic hormone, prolactin. Postpartum, the estrogen level drops off suddenly, and allows the release of previously inhibited prolactin which is now free to initiate the flow of milk. Sex hormones re-establish pituitary inhibition, thus arresting the lactating process.

In Fiskio's study,[1] "Premarin" with Methyltestosterone effectively relieved postpartum breast engorgement and suppressed lactation in 96.2 per cent of his group of 267 patients. Notably absent were breast abscesses, nausea, vomiting, excessive lochia, withdrawal bleeding or virilization. Menses were re-established after the normal six week period. The lack of mental depression during the puerperium was especially gratifying.

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Recommended Dosage: (Directions refer to *yellow* tablets.)

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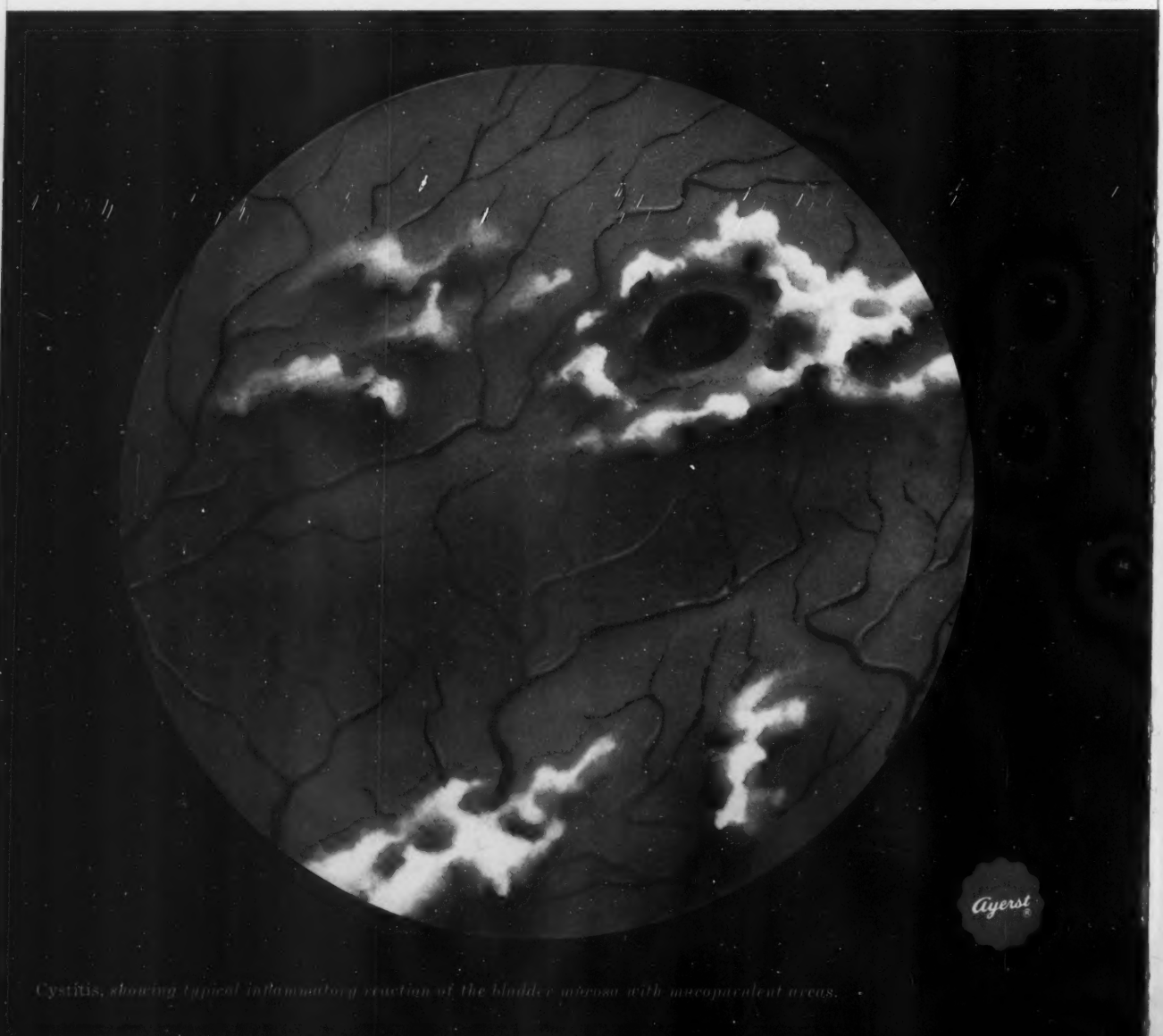

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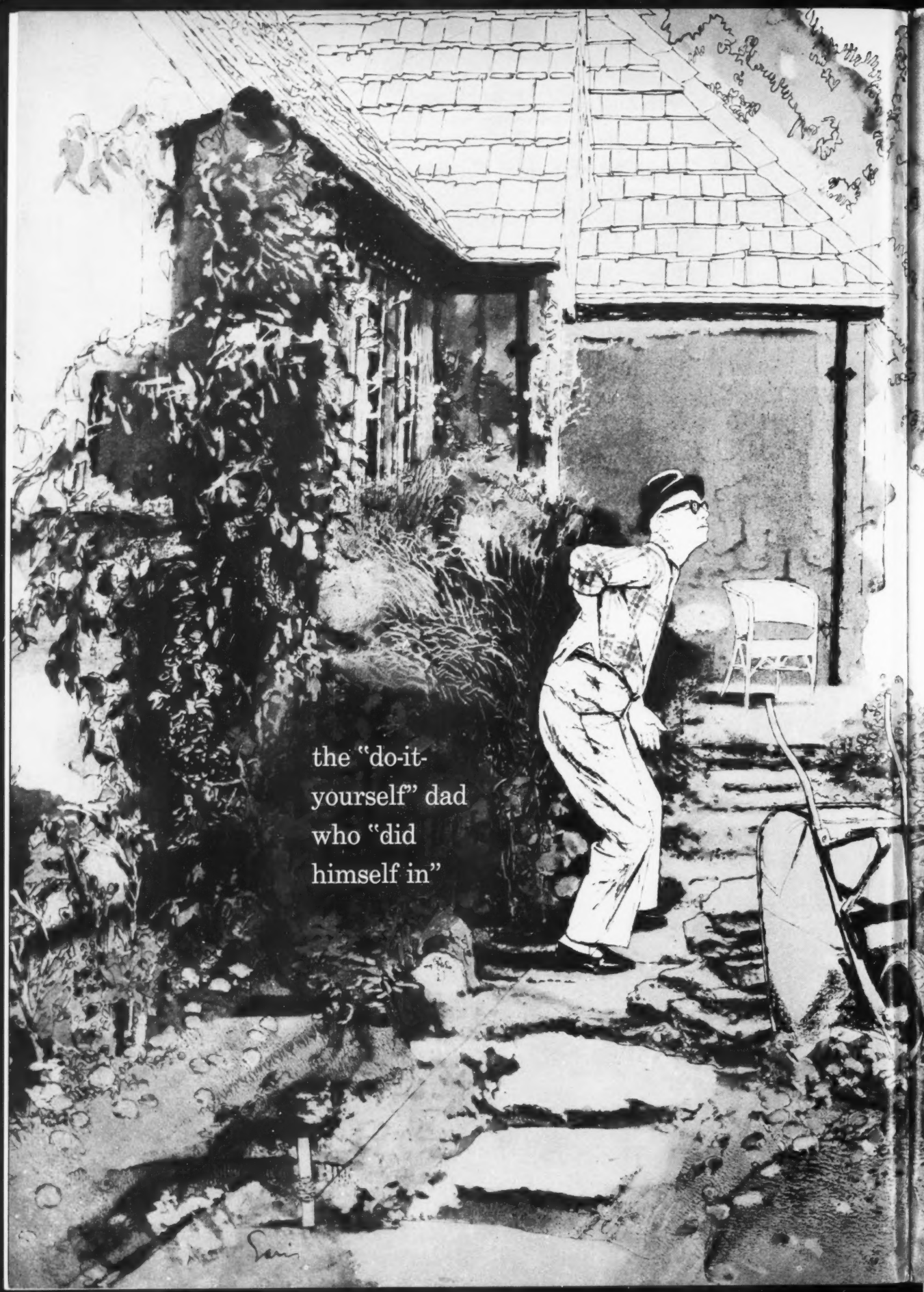
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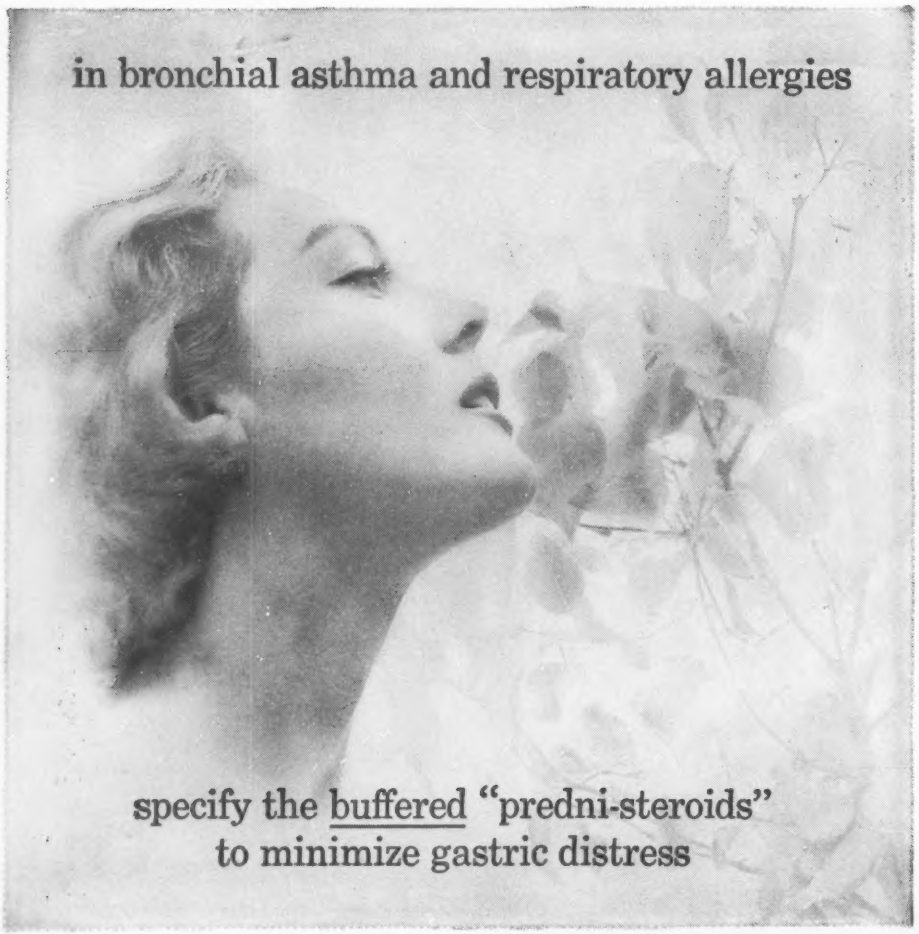

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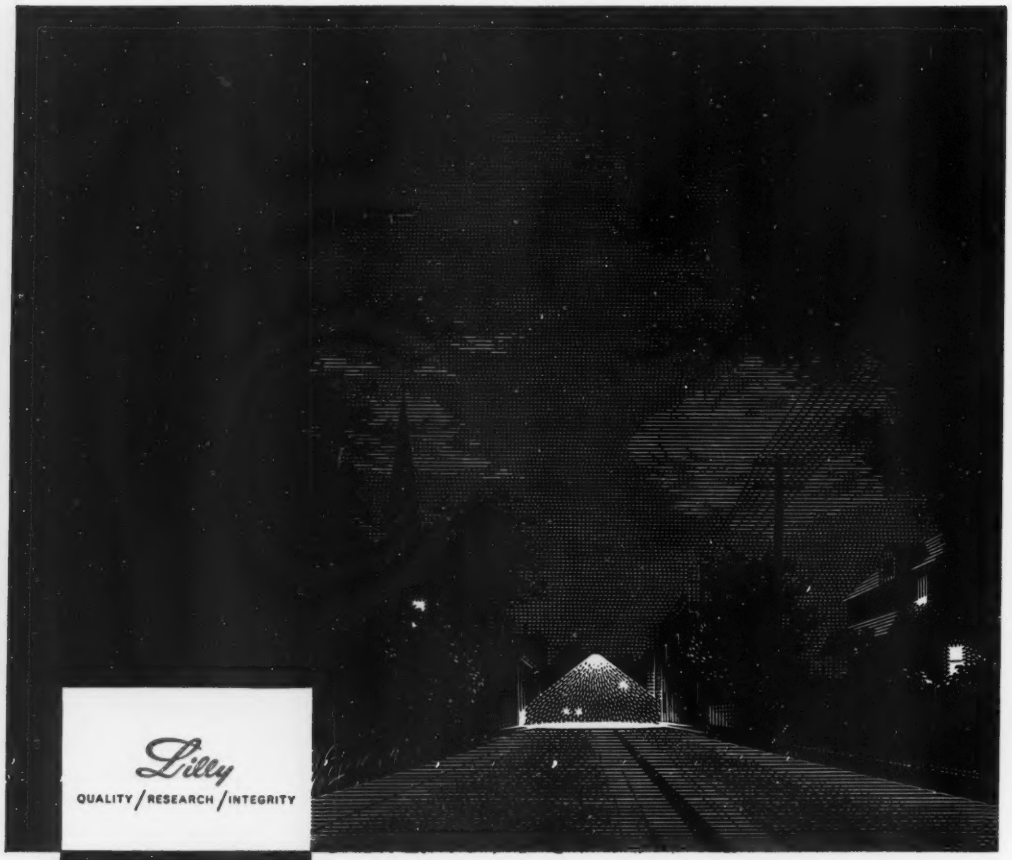

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Volume LVIII **SEPTEMBER, 1957** **No. 9**

Sodium and Potassium

Studies of Changes in Their Excretion Following Neurosurgical Operations

A. LOWENTHAL, M.D., A. SOETENS, M.D., *and* M. VAN SANDE, *Antwerp, Belgium*

Recent reports have focused attention on important modifications in electrolyte metabolism following general surgery and on ways of rapidly restoring the electrolyte balance in postoperative patients. So far, however, little has been done to study electrolyte balance in the postoperative period following neurosurgery. It is the purpose of this paper to report on changes in urinary excretion of sodium and potassium in 33 neurosurgical patients.

There are several means of investigating changes in body electrolytes, but all save one have distinct drawbacks. It is impractical to make repeated biopsies in order to investigate tissue content of sodium and potassium. It is also impractical, if not foolhardy, to do repeated spinal taps on patients who have just undergone neurosurgery. The great difference in potassium concentration between the red cells and the serum renders blood tests somewhat unreliable. Since feces contain less than 15 per cent of all potassium excreted from the body, feces analysis would not give valid results. Urine, therefore, is the most useful source of material.

The urinary excretion of sodium and potassium is undoubtedly modified by many factors: the age of the patient; his general state of hydration; the diet received in his postoperative period; his fluid intake and the administration of various medications and antibiotics; the type of anesthesia; the loss or retention of urine, and possibly the type of neurosurgical procedure. Since our study was performed on an active neurosurgical service, it was not possible to submit all of the patients under investigation to absolutely controlled conditions. Nevertheless, we hope to show that various patients, regardless of their age or sex, demonstrated comparable modifications of sodium and potassium metabolism as measured in their urine.

Neurosurgical intervention results in temporary modification of sodium-potassium metabolism in a manner similar to that observed following any type of surgery. These modifications are more apparent in patients who have undergone intracranial surgery than in those who have had surgery of the spinal canal. The modifications of potassium metabolism can be brought back to normal by the administration of potassium by mouth. The modification of sodium and potassium metabolism was not found in non-surgical patients who received artificial feeding and fluid therapy when comatose or semi-comatose.

From the biochemical research laboratories of the Institut, Bunge, Berchem-Antwerp, Belgium. The authors acknowledge the help of Charles M. Poser, M.D., University of Kansas Medical Center, Kansas City, who gave advice with regard to translation into English during his stay in Belgium as a Fulbright research fellow in neuropathology.

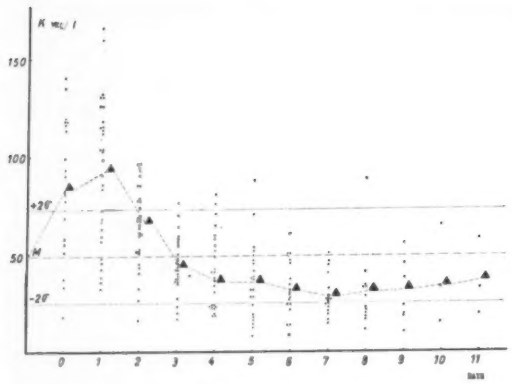

Figure 1

A variety of neurosurgical procedures were performed on the patients. There were 12 cases of spinal cord surgery comprising rhizotomy, removal of herniated nucleus pulposus, and operations on extra and intramedullary neoplasms. Eighteen of our patients underwent intracranial exploration for meningiomas, gliomas, posterior fossa tumors, and metastatic tumors.

Method of Investigation

Twenty-four-hour urine collections were begun four days prior to the operation and continued for ten days thereafter. The sodium and potassium content of each 24-hour specimen was measured

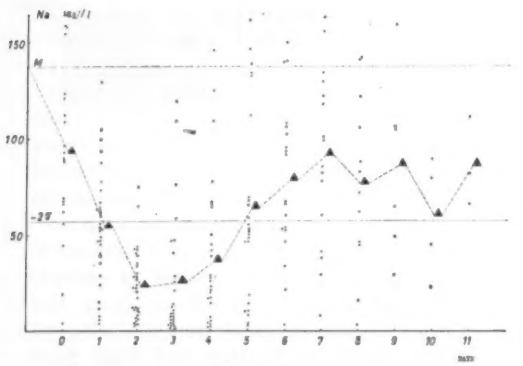

Figure 2

by the Perkin-Elmer flame photometer and expressed in milliequivalents. In addition to showing the absolute values of sodium and potassium, we employed the sodium-potassium ratio in milliequivalents as an expressive index of electrolyte change in the postoperative period.

Results

The over-all results are shown in Figures 1, 2 and 3. Figure 4 represents a typical pattern obtained in one case.

Figure 1 shows an increase in the elimination of potassium after surgery which starts during the first 12 hours on the day of operation. The excretion tends to be four times its average normal value. On the third postoperative day this excretion returns to a normal value, but then it continues to decrease as if to indicate retention of exogenous potassium by the organism.

Figure 2 indicates a decrease in sodium excretion which starts immediately after surgery and reaches its minimum value on the second and third post-

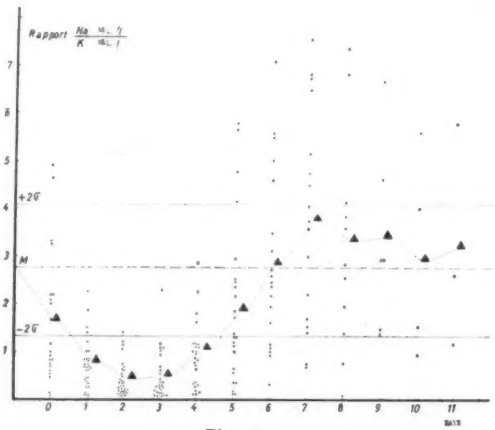

Figure 3

operative days. The sodium excretion then increases progressively, but it still remains below normal until at least the eighth postoperative day.

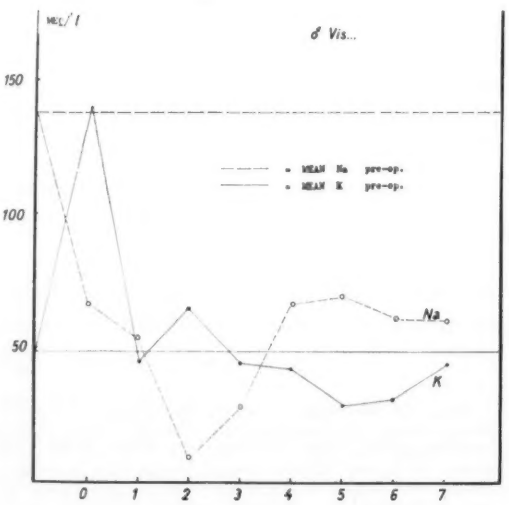

Figure 4

In the postoperative period, therefore, there seems to be an ionic retention which results in a decrease of the sodium and potassium elimination, although there is an initial transitory increase in potassium excretion which lasts approximately 24 to 48 hours.

In Figure 3 this ionic retention is shown by the sodium-potassium ratio expressed in milliequivalents. Before surgery this ratio has a mean value of 2.7 ± .7 (95 per cent of our ratios ranged from 1.3 to 4.1); following surgery this ratio decreases immediately and reaches a minimum value after the second postoperative day. By the seventh day the ratio has returned to its preoperative normal although both absolute potassium and sodium values are still low.

From these results we have drawn the conclusion that the patient's critical period with regard to electrolyte balance begins on the third postoperative day and lasts until approximately the eighth day, at which time he is considered to have regained his electrolytic equilibrium.

We have analyzed our cases of surgery on the spinal cord separately from those of surgery on the skull and its contents. The average lowest point of the sodium-potassium ratio in cases of spinal cord surgery is .40 and it ranges between .04 and 1.38. In only three instances did this ratio fall below .10. The first of those three cases was an intramedullary tumor which proved to be inoperable, in which the dura could not be closed; the second one was a high cervical exploration for paraplegia without tumor in a patient with an albumino-cytologic dissociation, while the third was an instance of epidural hematoma in a diabetic patient.

In our cases of intracranial surgery, the lowest values of the sodium-potassium ratio had a mean of .16 with a range of .02 to .54 with eight instances of the ratio being below .1. The high ratios were found

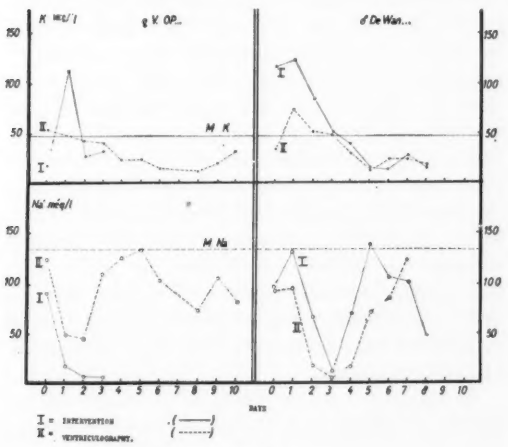

Figure 5

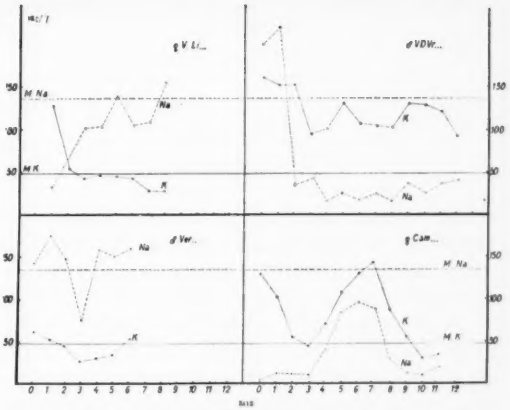

Figure 6

in a patient who had a biopsy of a left temporal glioma (.43) and an occipital lobectomy for glioma with an opening into the ventricle (.54). However, a patient who had undergone a biopsy of a left temporal glioma gave a very low value. Two patients who had had ventriculography and were not included in this series gave a ratio which never fell below 1.02 in the first case and .20 in the second. The sodium-potassium ratio reached its lowest value at somewhat different times during the postoperative period in different cases. The duration of the greatest drop in the ratio is also quite variable, and the significance of the variations is unknown.

Even though our results are so far incomplete, it would seem that intracranial surgical intervention modifies metabolism of sodium and potassium more severely than does intraspinal surgery.

We have had occasion to compare the change of sodium and potassium metabolism in two patients, first following ventriculography and then following exploration of the posterior fossa. In both cases no actual operative intervention was carried out. Figure 5 shows that the departure from normal was more pronounced in the patients after posterior fossa exploration than after ventriculography.

We carried out electrolyte balance studies in two patients who were not subjected to surgical intervention but who were semicomatose and receiving intravenous fluid therapy. Table I shows our results and demonstrates that even in patients who are in what superficially resembles a postoperative state there are no apparent modifications of sodium and potassium metabolism such as result from surgical trauma.

Discussion

We have been able to confirm the observations previously obtained by other researchers (Blixen-kröne-Moeller; Snyder and Snyder; Randall, Habif,

TABLE I

	Date	K mEq/L	Na mEq/L	Na/K ratio
case A	1/5	61.5	25.6	0.41
	1/6	63.5	47.0	0.47
	1/7	52.7	103.0	1.94
	1/8	47.4	108.0	2.30
	1/9	40.4	91.0	2.26
case B	1/10	50.9	68.0	1.34
	1/13	42.0	127.0	3.01
	1/14	54.5	153.0	2.80
	1/16	46.9	167.0	3.59

and Lockwood; Woringer, Baumgartner, and Lienhart). These authors reported an increase in potassium elimination during the first two or three days and a decrease in sodium excretion toward the fourth postoperative day in cases of general surgery.

It has been said that the change in urinary potassium excretion parallels destruction of tissue through surgery. Several authors, however, have shown that the nitrogen loss does not follow the same curve as the potassium loss in urine (Lans, Stein, and Meyer, and Elman, Shatz, Keating, and Weichselbaum); therefore, it seems hardly logical to accept the severe potassium loss immediately after surgery as being the direct effect of tissue destruction. In our own cases we have observed a considerable increase in potassium excretion in the course of only a relatively minor tissue injury such as that incurred by placing a ventricular drainage tube.

Other authors have tried to explain the modification of sodium-potassium metabolism on the basis of an alarm reaction dependent upon endocrine mechanisms. Interesting work along this line has been published by Gros, Minvielle, and Vlahovitch. These authors plotted a curve of the total blood eosinophile count after neurosurgical operations, which seems to be remarkably close to the variation curve of the sodium-potassium ratio we have observed. This tends to support the hypothesis that electrolyte modifications are indeed related to a stress reaction and that increased potassium elimination in the urine and hypokalemia are the result of a potassium deficiency in the tissues following surgery. It has been demonstrated by Blixenkröne-Moeller and Evans that serum potassium levels are poor indicators of the actual metabolism of potassium in the postoperative period. The report published by Eliel, Pearson, and White on measurements of potassium in muscle biopsy specimens seems to support this contention.

Wise has recently published an article on the changes in potassium and sodium metabolism following neurosurgery. He noted loss of potassium and retention of sodium, but he did not make clear the time relationship of these metabolic changes. He has reported his observations in five cases, of which three were chromophobe adenomas with endocrine changes, one was a cerebellar tumor with increased intracranial pressure, and last was a case in which ventriculography was performed for unlocalized increased intracranial pressure. These cases somewhat resemble the ones analyzed by Cooper. Wise's bibliography is extensive.

The most striking change in electrolyte balance during the first hours after surgery is the increased elimination of potassium. It is conceivable that this results in the eventual decrease of sodium elimination by bringing about an actual loss of cellular sodium. However, before accepting this hypothesis, the following facts must be considered:

A. Some urinary excretion of potassium is necessary, since it never falls below a certain minimal value in normal individuals.

B. Sodium excretion in the urine seems to be much more variable and may in certain cases be almost nil.

C. The increase in potassium and the diminution of sodium in the urine do not occur simultaneously, nor do they follow a linear relationship.

D. We have found that correcting the loss of potassium may either abolish the sodium retention, diminish its importance, or postpone its occurrence.

We administered potassium by mouth to four of our patients. The resulting curves of elimination of sodium and potassium and the variations of the sodium-potassium ratio in the urine are shown in Figure 6. The administration of potassium by mouth (10 grams of potassium chloride per day) did not result in an exaggerated loss of potassium in the urine. On the other hand, in one case it seemed to have brought the sodium-potassium ratio back to the normal range after the third day.

In a second case (Cam), the sodium-potassium ratio, which had been maintained at a normal range for eight days by administration of potassium by mouth, fell to an extremely low value when potassium was stopped, and was again brought back to normal when potassium administration was resumed. In case Ver (a patient who was a poor operative risk), the sodium-potassium ratio remained high and the excretion of sodium remained low despite treatment. In case Vdv, the administration of potassium chloride was rather irregular, and the results were less definite, especially in view of the fact that the patient developed postoperative infection which necessitated the administration of many medications, including antibiotics.

In patients receiving potassium by mouth the excretion of potassium in the urine after neurosurgery

(Continued on Page 626)

Tuberculosis in Kansas

A Study of Its Past, Present, and Future

MARTIN J. FITZPATRICK, M.D., ***Kansas City***

To visualize more clearly the position of tuberculosis in Kansas today, and to consider some of the changes that probably await us in the future, it would appear wise to review briefly some of the events relating to this disease that have taken place in this state since it was formally constituted in 1861.

During the period of migration of eastern and middlewestern pioneers to Kansas in the last third of the 19th century, there is no known record of the extent of tuberculous infection in this state. At that time there was no official organization to record or to deal with the majority of public health problems on the frontier.

The first changes in tuberculosis control in the new state of Kansas probably had their impetus from the organization in 1904 of what is today the National Tuberculosis Association. Dr. Samuel J. Crumbine, first secretary of the Kansas State Board of Health, attended several of the early organizational meetings of the N. T. A. on the eastern seaboard. In 1907 an International Congress on Tuberculosis was held in Washington, D. C. At that meeting Dr. Crumbine met and discussed tuberculosis and related topics with such outstanding leaders as Trudeau, the American pioneer; Koch, the discoverer of the tubercle bacillus, and Calmette, the French leader in tuberculosis research at that time. Dr. Crumbine returned to Kansas filled with enthusiasm for organizing a tuberculosis program in this state. He received a sympathetic ear from Governor E. W. Hoch and suggested that a meeting of all interested citizens be called to organize a tuberculosis control program.

The first formal meeting concerned with this disease in Kansas was held on December 3, 1908, at the state house in Topeka, and from this the Kansas Association for the Study and Prevention of Tuberculosis, the parent of our present state tuberculosis society, was formed. In 1908 the first Christmas seal sale was held in Kansas, with an extremely modest yield. Gradually, through the years that followed, a corps of dedicated volunteer tuberculosis workers grew in Kansas, to the extremely effective level that exists today across the state.

One of the early points for emphasis established by the leaders of the budding national organization, especially Dr. Trudeau, was the need for health education of all people. As early as 1905 he had stated, "The first and greatest need is education—education of the people, and through them, education of the state." In retrospect that was a most intelligent move, for the problem of tuberculosis far exceeded the knowledge, skill, or interest of the medical profession of that day. Its ultimate control depended on solving the major social and economic problems that could only be dealt with by combined interest and action of individuals from all walks of life.

With the stimulus of this new organization attempting to control tuberculosis in Kansas, the state legislature in 1911 enacted a law authorizing the creation of a state sanatorium for the treatment of this disease. In that year they appropriated $50,000 "to be used to purchase the proper site, to erect and to equip the necessary buildings, and to pay the running expenses for a period of two years." It is of interest that a tract of 240 acres just two miles west of Newton, in Harvey County, was selected to be the site for the sanatorium. Some difficulty was encountered in obtaining possession of the land, and the matter was still unsettled when the 1913 legislature convened. That body repealed the old law and enacted another, which further provided that the sanatorium be located in any county where 160 acres of land would be donated free of charge to the state.

Following this, an advisory commission and a superintendent toured many counties of Kansas looking for the site for the new tuberculosis sanatorium.

Many changes have taken place in tuberculosis therapy in the past 50 years. Today's chemotherapy can be administered by any practicing physician. Although hospitals for the care of tuberculous patients are still necessary, physicians at those institutions are no longer caring for the majority of patients with the disease. Future control of tuberculosis in Kansas will depend more on the practicing physician than it has in the past.

Presented at a meeting of the Tri-County Medical Society, Newton, June 3, 1957. Dr. FitzPatrick is president of the Kansas Trudeau Society.

In July 1913, while the group was in Norton County, the businessmen of Norton approached them and told them to select whatever area in the county they liked best with the understanding that this land would be given to the state. They promptly took up this generous offer, and "160 acres of fine land" were donated. Another 80 acres were later purchased, thus making a total tract of 240 acres.

Construction of the sanatorium was started in October 1913, and the cornerstone of the first permanent building was laid in June 1914. The first pavilion was completed in September 1914, and the new sanatorium was opened as a 16-bed unit in February 1915, with Dr. C. S. Kenney as superintendent. From this rather humble start, the hospital grew steadily and assumed a most important role in treatment of this disease in Kansas.

In 1908, when the Kansas Association for the Study and Prevention of Tuberculosis was first organized, there were approximately 5,000 cases of active disease in this state with a population but a fraction of today's. Early statistical reports suggest that more than 100 people died from this disease in Kansas every month. Some 30 year later, by 1938, even before the advent of modern therapy, the death toll in Kansas had dropped to around 428 per annum. By 1941, Kansas was among the six states with the lowest annual death rate from tuberculosis. This decline in tuberculosis mortality was actually a nationwide one, representing a true triumph of preventive medicine and improvement of living and working conditions across the country at large.

During this time other advances in the changing picture of tuberculosis in Kansas were evident. In 1941 the legislature, looking at the major problem of silicosis and tuberculosis in the southeastern corner of the state, started the long road of legislative action that eventually resulted in building a modern tuberculosis hospital at Chanute, to deal with severe local problems of tuberculosis and silicosis. Other changes have included the appropriation of funds to build a modern unit at the University of Kansas Medical Center, to serve as a center for the teaching and training of future doctors and nurses in a changing approach to tuberculosis and other pulmonary diseases. An important aspect of this new approach to the teaching of pulmonary disease was the early recognition by the Kansas Tuberculosis and Health Association of the need to endow a full-time chair in this specialty at the university, a program that is now being followed by other states.

It might be well to consider what has happened to the picture of tuberculosis outside Kansas, and to reflect briefly on major advances in treatment of this disease that have revolutionized our approach to it. By reflection on events that have taken place in the recent past, we often can get some inkling as to the future course of tuberculosis control both in the nation and in this state. Let's go back some 50 years to the start of the 20th century.

At that time tuberculosis was the number one killer of our civilization. This was most marked in cities along the eastern seaboard, but it gradually also became a problem of other areas as the rising tide of population moved westward. As we have seen, this great problem of tuberculosis actually brought into being the national, state, and local volunteer groups that were to deal so effectively with it. Some 50 years later, the fruits of this effort are readily apparent by the striking decline in tuberculosis across the nation. Along with great changes in the picture of this disease in human beings, the once formidable problem of tuberculosis in cattle has been practically eliminated. All of this occurred before there was a specific form of treatment for this disease.

The major approach to treatment of patients ill with this disease prior to World War II, was in the use of non-specific regimens; bed rest and collapse of diseased lung. Rest, of course, was the major form of therapy up to that time, that had been effective in restoring some patients to a useful and a fairly healthy life. If cavitary disease was present, artificial pneumothorax was the most widely used form of collapse treatment. It has been estimated that three-fourths of all patients entering a tuberculosis sanatorium prior to the advent of chemotherapy received pneumothorax at one time or other. In patients with more severe cavitary disease which resisted collapse by pneumothorax, or with a complication of pneumothorax, the major surgical procedure resorted to was primary thoracoplasty. By removing ribs, the destroyed lung with its cavities would then be allowed to retract and, thus enhance healing in the resting lung.

During the years preceding World War II, tuberculosis patients were removed from their home environment, principally from cities where the disease was most rampant, to be treated for prolonged periods in rural, isolated sanatoria. The healers of tuberculosis consisted of a small group of physicians and nurses in these sanatoria whose interest in this disease had been aroused, usually by having been victimized by it. After a patient was discharged, follow-up was conducted primarily at the sanatorium when this was physically possible, or in some centrally located chest clinic, often in the community in which the patient lived. Very strong ties were thus established between the majority of tuberculosis patients and the physicians treating this disease. In general, active tuberculosis patients were shunned by most physicians in everyday practice. It evolved that only a few physicians were either capable of or interested in treating the large army of tuberculous individuals.

The first great change in this rather peculiar form of medical practice was one that was largly unnoticed at the time by most tuberculosis workers. It was the demonstration of the marked anti-tuberculous activity of streptomycin by Schatz, Waksman, and co-workers at Rutgers University in the early 1940's. Following this brilliant discovery, clinical trials were performed in many areas throughout the country, and it was soon established that streptomycin was the most effective substance known to date capable of altering the course of tuberculosis. We are all familiar with the early drawbacks that were soon found with this drug, its expense, impurity, eighth cranial nerve toxicity, and the early emergence of bacterial resistance. All of these factors at first limited the widespread use of this new drug in treating tuberculosis—a chronic disease often spread over many years.

The next significant step in the evolution of modern treatment of this disease came from Sweden in 1947, with the demonstration by Lehman and coworkers of the anti-tuberculous effect of para-aminosalicylic acid (PAS). These scientists demonstrated that this new drug was effective in patients who had developed streptomycin-resistant organisms as well as in the sensitive patient. PAS was also found capable of delaying the emergence of streptomycin-resistant bacilli, when used in combination with this more potent drug. For the first time we were able to prolong the anti-tuberculous effect of streptomycin and to delay, and in some instances to prevent, the emergence of resistant organisms. Thus, chemotherapy of tuberculosis advanced beyond short-term use to control critical emergencies into the area where drug therapy could be given for periods of a year or more, if needed.

Large scale clinical trials were conducted in this country by the U.S.P.H.S. and the Veterans Administration and in England by the British Medical Research Council. From them, the regime of combined streptomycin and PAS emerged by 1951 as the standard form of treatment of tuberculosis of all organ systems. At this time most patients were receiving tuberculosis chemotherapy in sanatoria or hospitals designed for treatment of this disease, and little treatment was administered outside of these few institutions.

This situation was profoundly changed in a few years by demonstration of the great therapeutic effect of isoniazid (INH) in tuberculosis patients early in 1952. This new synthetic drug was found to be even more effective than streptomycin in treating the disease. In the years that followed its introduction, various regimens were studied in many clinics throughout the country. It was noted that isoniazid could be used in combination with either PAS or streptomycin and that this drug diffused readily into the central nervous system and appeared in high concentration in the cerebrospinal fluid. Thus, it became an extremely effective agent in the treatment of tuberculous meningitis, and no longer did physicians have to resort to intrathecal administration of streptomycin in these patients.

These and other changes in treatment of tuberculosis within the past decade have had a profound effect on the older and more non-specific forms of therapy. Today we are seeing studies suggesting that strict bed rest is no longer necessary for most patients, and that it actually may do harm in certain types of tuberculosis in children. We have witnessed the almost complete removal of artificial pneumothorax as a form of treatment in this country. We have seen the development of resectional surgery of tuberculous cavities and other lesions, a form of treatment that could not be carried out before appropriate drug therapy was available. And, of course, we have seen the relentless prolongation of drug therapy in this most chronic of all infectious diseases. From this latter event we now have evolved a method of treatment that can be considered truly "curative" in most patients if properly used.

Another product of the development of adequate chemotherapy, most marked in the years since the advent of isoniazid, has been the fact that treatment of tuberculosis has been removed gradually from the hands of a few and placed in the hands of any physician in the United States. This phenomenon has naturally caused considerable reaction and comment on the part of some physicians who are responsible for the treatment of patients in tax-supported sanatoria and in tuberculosis control movements across this country. But despite the majority of these sentiments, home treatment of tuberculosis patients is here to stay, and it will continue and increase in future years because of basic economic and human factors.

Along with these significant changes in the treatment of this disease, we have witnessed others in the composition of the group of patients with tuberculosis. The past 20 years have seen a gratifying reduction in incidence of this disease in younger members of our population, with a proportional rise in the problem of tuberculosis in older people. Today in most of our tuberculosis hospitals a majority of our complicated patients are in the age range of geriatric problems. This means that today's hospital treating these patients must be better equipped, better staffed, and better administered than it was a decade or two ago. These older patients often have other diseases combined with and complicating tuberculosis. This trend will increase in the future, with the continuing prolongation of the life-span of our population.

Against these remarks concerning the past and the

present, it might be well to try to visualize what some aspects of our tuberculosis program of the future will look like. This attempt at clairvoyance is divided into three categories, as outlined below.

1. *Case Finding*—With the decline in morbidity and mortality from tuberculosis in most of our communities across the nation, including Kansas, the future problem of finding new cases early in their course will become more complicated and more expensive. New techniques that are most suitable to each local community will have to be evolved. It is becoming apparent from many studies that mass chest x-ray surveys on a statewide basis are no longer the most efficient nor the least expensive way of finding latent active disease. This effort will probably be replaced gradually by a continuing x-ray survey of those members of the population who statistically have the highest prevalence of infection. Today's x-ray survey will also be fortified in the future by wide-spread tuberculin skin testing programs, again on a continuing basis. From these tuberculin converters, the follow-up on household contacts should be quickly done, and thus the asymptomatic case of tuberculosis will be ferreted out from the general population early in its course.

2. *Treatment*—The number of patients with active pulmonary tuberculosis being treated by physicians outside our hospitals will increase in the future. This will occur despite the protests of physicians or public health workers, and all should honestly recognize this fact. Thus, it would appear wise to try to determine which patients will benefit most from home treatment, and which individuals can be best handled in the hospital. Certainly individuals with demonstrated cavitary disease, or a persistently positive sputum that fails to convert quickly on drug therapy at home, or patients with another significant complicating disease, should be referred early in their course to a hospital specializing in treating tuberculosis. A closer liaison between the family physician and the tuberculosis hospital to insure continuity of management will be of paramount importance.

A fundamental principle of management should be that most patients, including those with tuberculosis, are best cared for whenever possible in their home environment, if it is adequate. This of course, must always preclude the infection of others, for this is still a communicable disease. When this principle cannot be carried out adequately at home, the patient must be isolated until non-infective. Since we are dealing with sick and complicated human beings, this temporary isolation will be accepted more readily if near to the patient's home.

As chemotherapy becomes more effective, as our use of it becomes wiser, and as our tuberculosis case finding becomes better, especially in younger individuals, the number of surgical resections performed for persistent tuberculous cavities will diminish. Indeed some studies already demonstrate that there is no true difference in the patient's course whether or not closed tuberculous lesions are resected or left behind, provided prolonged continuous chemotherapy is used. In the future, surgical treatment of tuberculosis will be more in the nature of a "salvage operation" on an older patient with advanced disease, often with other limiting cardiac and pulmonary factors. Thus, surgical treatment of tuberculosis will tend to become a more difficult problem and will require a team approach to deal with the complicated patient in need of operative help.

3. *Physicians*—In the past there has been a dedicated and highly trained group of physicians who have banded together, mostly in rural sanatoria or other tuberculosis hospitals, to treat most patients with this disease. To these pioneers we owe a great debt, for from them have evolved most of our skill and knowledge concerning today's medical and surgical management of patients with pulmonary disease. It has often been stated in recent years that this group of physicians will disappear; that since the problem of tuberculosis is diminishing and the scene of its treatment is changing, physicians specializing in the treatment of this disease will ultimately "go out of business." In part this is true, for the physician of today and tomorrow will no longer be able to specialize in just the treatment or management of tuberculosis because of many of the factors already mentioned. Instead he will, of necessity, have to be skilled in the differential diagnosis and appropriate management of all abnormalities of the chest that can simulate this "great imitator."

In the past, when tuberculosis was the number one killer, it was also the prime cause of pulmonary pathology in most instances. In recent years, with the decline in mortality from this disease, other problems of the lung have assumed a greater importance and will continue to do so. Thus, the physician of the future will have to be more accomplished in the broader field of pulmonary disease than his forefathers were. There will always be a need for skilled physicians in this specialty, however, to deal with the more complicated diagnostic techniques as they evolve, and to aid in their interpretation and use in patients referred by other physicians.

I have not so far touched on the recent Kansas tuberculosis study conducted by Dr. Joseph Stocklen and a team of national experts. I think the details of this study are well known to most of you. One of the important things to come from this study is that we now have some idea of where we stand and in what direction we should be moving. Although Kansas is blessed with a low tuberculosis mortality

and morbidity rate as compared with the national figures, it is still too high.

It should be hoped that the number of tax dollars appropriated to take care of today's tuberculosis problem in Kansas can, in the future, be partially directed into other areas. It is also hoped that by streamlining and modernizing our entire tuberculosis program at all levels, this problem can ultimately be more efficiently and less expensively dealt with. However, tax funds will always be required to control this and other communicable diseases in Kansas.

There is little question that the sanatorium at Norton and other comparable facilities in the state will undergo changes that will be dictated by changing medical and social necessities in Kansas. It would also appear logical that some day an appropriate tuberculosis unit will be established as a part of a general hospital in Wichita, in the major center of population and, presumably, of potential tuberculosis in this state. From the Stocklen report we have learned that the major outstanding problems of tuberculosis in Kansas still are confined mainly to its three largest cities and to Cherokee County.

We have also learned of disquieting flaws and defects in our continuing public health surveillance of this disease. The large number of known active tuberculous persons in Kansas, not under adequate medical supervision, augurs for an ever greater future seedbed of disease. Changes in the picture of tuberculosis in the past decade can only breed continuing problems until the known sources of infection in our communities are identified and controlled. The recent modernization of our recalcitrant patient law is a step forward against the problem of continuing community infection.

By knowing where our problem is greatest, we can assume a more aggressive program aimed at early detection, adequate treatment, and total rehabilitation of the patient and his family. To accomplish this will require an integrated program combining the skills and accomplishments of medical science, social study, enlightened legislation, and economic assistance both in these communities and across the state at large.

But no program in combating this disease will succeed without the understanding, cooperation, and active support of all physicians in Kansas, for the future control of this disease will rest more squarely on the shoulders of the practicing physician than at any time since Hippocrates.

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Coarctation of the Aorta

Complications of Abdominal Pain and Distention after Surgical Resection

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Interest in presenting this case was stimulated by an excellent article in the June 1956 issue of the *Journal of Thoracic Surgery*. The article, "Abdominal Pain following Surgical Correction of Coarctation of the Aorta: A Syndrome," was by Dr. Dean M. Ring and Dr. F. John Lewis of Minneapolis, Minnesota. A discussion of the cause of the abdominal syndrome was followed by 18 case reports. Also mentioned was a case presented by Perez-Alvarez and Oudkerk.

We wish to add our report to the literature since many such complications will probably occur in future surgical correction of this aortic abnormality. Another reason for presenting this case is that our patient had an additional complication—atony of the bladder—necessitating an indwelling catheter for a prolonged period of time.

Our patient, C.S., a four-year-old boy, was found to have hypertension of 210/110 in the right arm and 200/100 in the left arm. He had had repeated bouts of upper respiratory infections throughout his

The patient reported here, a four-year-old boy, benefited from surgery although complications followed the operative procedure.

life and had complained of weakness, fatigue, and cramping in the legs. Examination revealed absence of pulsation of the femoral, popliteal, posterior tibial, and dorsalis pedis arteries. No popliteal blood pressure was obtainable. The typical purring sensation was felt on palpation of the back, and a humming type of murmur was heard on auscultation. Kidney function studies were normal. A diagnosis of coarctation was made, and surgery was performed on April 17, 1956.

The thorax was opened through a posterior lateral incision in the fourth interspace. Extensive collateral arterial circulation was encountered when the chest wall was opened. The intercostal branches were isolated, ligated, and transected. The recurrent laryngeal nerve was carefully retracted to avoid injury. The ductus was clamped and transected and found not to be patent. The coarctation was then resected, and the aorta was easily resutured. The diameter of the coarctation measured approximately one millimeter. Little bleeding was encountered after the clamps were loosened, and it was easily controlled by pressure. Satisfactory pulses were found in the femoral and dorsalis pedis arteries. The blood pressure at the end of the operation was 140/90. The thorax was closed in the usual manner with an intercostal drain to promote re-expansion of the lung. The patient left the operating room in excellent condition.

Postoperative progress was satisfactory, and the patient voiced the usual complaint of pain in the chest. He also had pain and difficulty in voiding, and after the third day a decreased urinary output was noted. On the fifth day his output measured only 250 cc., so an indwelling catheter was inserted.

On about the fourth day he began complaining of cramping pain in the epigastrium. The next day there was noticeable distention of the abdomen, and the intestinal sounds suggested the possibility of obstruction. X-ray of the abdomen on the sixth day showed dilated loops of small intestine. The abdomen was still distended, and peristaltic waves could be seen on the abdominal wall. Gastric suction and parenteral feedings were instituted. Carefully calculated electrolytes and fluids were administered intravenously, and he was maintained in normal balance.

On his 11th postoperative day the distention had entirely cleared, and he was passing gas rectally. Gastric suction was then discontinued, and he began taking food by mouth. The indwelling catheter was removed, and the patient began urinating without difficulty. During the period from the fourth to the 11th postoperative day his temperature rose to a high of 102 degrees.

The day after resection of the coarctation, blood pressure of both arms and legs was around 170/110. On the fourth postoperative day Apresoline was started to reduce his blood pressue. It had returned to a level of 110/70 in both arms and legs four days later, so Apresoline was discontinued and the blood pressure did not become elevated again.

After the 11th postoperative day the patient's progress was entirely satisfactory. He was ambulatory and was given a progressive diet. He was dismissed from the hospital in excellent condition on his 15th postoperative day.

The child was still in excellent condition when examined in the office six weeks after surgery. Arm blood pressures were 110/70 and popliteal blood pressures were 100/60. His mother stated that he was active and no longer complained of fatigue or aching in his legs.

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Childhood Granulomas

Report of a Case of Obstructive Growths in the Ear Canals

JOSEPH A. BUDETTI, M.D., *and* ERNEST M. SEYDELL, M.D., *Wichita*

Among unusual and deceptive conditions which occasionally confront a physician, none can be so baffling as a granulomatous lesion of the ear canal in a one-year-old child. Chronic ear discharge in an infant suggests any number of possible causes, some of which can be a simple medical problem while others can be serious surgical emergencies with all grades between.

The external ear can show eczema, ulcerations, or epidermal infection. The canal may show foreign bodies, impacted cerumen, external otitis of pseudomonas, staphylococcus, fungus or allergic types; granulomas or aural polyps may protrude through drum perforations. Middle ears can show chronic discharging infections through perforations of the drum with or without polypi, as well as allergic exudates. Finally, the mastoid itself may be the basis of the drainage and middle ear granulations.

In our patient, both ear canals were blocked by large papillomatous growths behind which thick, purulent, creamy exudate accumulated. The 21-month-old child was first seen in August, 1955, with a history of drainage from both ears since having a head cold eight months previously. He had been under medical treatment by two different physicians for what gave every indication of being a routine case of bilateral otitis media. Ear drainage had been constant, malodorous, and creamy purulent. Other symptoms were occasional pain and frequent "pulling on the ears" by the child.

The parents were not conscious that the child had suffered a hearing loss since he responded normally to conversation. There was a family history of asthma but no history of allergy in the patient except hives from penicillin. The mother stated that various parenteral and oral antibiotics had been used repeatedly and extensively but could not identify them by name.

On the first examination nothing could be seen because of complete obstruction of each canal by large granulomatous masses bathed in pus. They resembled aural polyps in consistency. The nose and throat were negative except for enlarged tonsils and adenoids. X-rays of the mastoids were surprisingly normal with fair pneumatization even at this young age.

Under general anesthesia the masses were removed by the use of an aural snare and cup forceps. The drum appeared to be intact on the left but indistinct on the right because of bleeding. Gauze packing was inserted in each ear. Culture of the discharge showed hemolytic staphylococcus only moderately sensitive to two antibiotics and sulfa. Microscopic study showed granulomatous tissue with none of the suspected papillomatous element. Terramycin was given parenterally at first, orally later. The gauze packing was replaced twice on alternate days but was then discontinued because the granulomas appeared to be controlled. Both drums were then seen to be essentially normal.

About two weeks later the discharge recurred and the granulomas reappeared rapidly thereafter. Medication with terramycin was resumed, then changed to syrup Gantrisin. The granulomas were cauterized every four to seven days. Caustics used to no avail included lactic acid, silver nitrate, and Podophyllin in that order. Biomydrin drops were prescribed for local use. By November 29 the right canal was half filled and the left completely filled by papillomatous masses similar to those originally found. Surgery was repeated and both canals were cleared.

Surgical removal followed by pressure packs and simple local therapy proved effective in combating bilateral obstructive staphylococcic epithelial granulomas in a 21-month-old boy. Antibiotics, administered orally and parenterally, were ineffective.

The focus of each mass seemed to be midway within the canal at the posterior superior junction with dehiscence of the canal epithelium down to the mastoid bone. The drums were seen to be intact. After excision of the masses, a tightly rolled cotton pack impregnated with Polycin-Otosmosan solution was fitted snugly into each canal. The pathologist again reported the tissue as granuloma with no evidence of papillary stalk.

This time the packing was replaced every other day and fitted quite snugly for pressure. It was continued for three weeks. No oral or parenteral antibiotics were used. After the third week healing appeared complete. Monthly rechecks for the next eight months showed no recurrence. Both canals epithelized well with minimal cicatricial contraction on one side and normal canal on the other. The drums have remained intact.

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Wichita 2, Kansas

PRESIDENT'S PAGE

DEAR DOCTOR:

Fee schedules have provoked much discussion, especially quite recently. Such schedules arose in Blue Shield and insurance plans, compensation laws, VA schedules, and currently Medicare.

Medical societies have been urged to approve fee schedules to establish "usual" fees (whatever "usual" fees are). Former A.M.A. president Ed McCormick sponsored such standardized fees, urged their adoption and publication. But the underlying reasoning is difficult to follow, and widespread professional acceptance has not ensued.

However, the medical society of Erie County, New York, has compiled a schedule of "usual or customary fees." They state, "In all cases of disputes—coming to the Mediation Committee—fees or charges in excess of the customary fee will have to be justified." Hmm!

Are medical services mere commodities salable at so much per each? Are diagnoses, medical judgment, knowledge of proper therapy, surgical skill, of fixed value regardless of who presents them? Regardless of talents, experience, skill, degree of successful accomplishment in one's profession? Is it not fatuous to assume a fixed value for medical service whether it follows a brief training or a five-year residency, whether from scant experience with few cases or from extensive experience in a particular field? Certainly in a freely functioning professional climate the intelligent patient does so conclude.

Ohio doctors refused to sign a Medicare contract with a fixed fee schedule. They say it violates their fundamental principles. Interestingly, they are, nevertheless, partaking in the program. The Defense Department is paying each Ohio doctor the statement he presents showing *his* "usual" fee. The results are reported as quite satisfactory, that fees average very close to the prepared schedules and no abuses are mentioned.

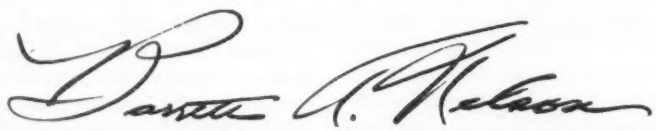
There is a Wisconsin Blue Shield plan without a fee schedule. It pays each doctor *his* "usual" fees, with expected variations. A few abuses were reported; a few took an unfair advantage. To teach the few the facts of life has not proved too difficult. The costs to the plan are said to approximate those of comparable plans with set fee schedules.

The California Medical Society conducted a thorough study, found there was no such thing as a "usual" or "customary" fee. They very ingeniously contrived a "Relative Value Schedule" to indicate by use of proportionate unit numbers, the relative values of various procedures. Our Fee Committee would do well to adopt a similar schedule.

Kansas doctors rejected the proposed $6,000 Blue Shield contract. Too many felt the fee schedule would establish rigid, inflexible, set fees for all of Kansas and (rugged individualists) they refused to go along.

One wonders if the valiant physicians of Ohio and the Wisconsin group may not have the ultimate solution. Might such a Blue Shield plan without a fee schedule be the ideal answer for Kansas? If, as it purported to be, the $6,000 plan was based on the "going rates in Kansas," then the proposed subscription charges should furnish ample funds to pay each physician his ordinary charges just as he applies them in his daily practice. Maybe we should consider such a plan and give it careful thought.

Fraternally yours,



President

EDITORIAL COMMENT

Medicare

Sufficient experience has been obtained under the Dependents' Medical Care Program that the Kansas Medical Society's special Committee on Medicare issues the following statement on some common misunderstandings.

Medicare is a program to assist the dependents of service men and women in all branches of the armed forces. Under limited circumstances which have been carefully defined, the federal government will purchase the services of civilian doctors to care for dependents of service personnel. A short definition always fails to include every possibility, but the following statements are almost correct, at least so much so that a lengthy explanation would be required for the very few exceptions.

Medicare is a program for hospitalized patients. The government defines a minimum hospital stay to be not less than 18 hours unless, after surgery, the patient is discharged in less time, or unless death occurs in less than that period.

There are a few exceptions in which a patient may receive benefits under Medicare and not be in a hospital. The first of these is obstetrical care. The patient may be delivered outside a hospital. If this is done, the patient pays the physician directly the first $15, and Medicare pays the remainder up to the maximum allowed according to the fee schedule.

The second exception is in the care of accidental injuries which are limited to fractures, dislocations, lacerations, and other wounds. Here also the patient pays the first $15 if care is rendered outside a hospital. It should be noted that emergency care outside the hospital does not necessarily qualify for Medicare payments.

The third eligible service for care outside a hospital has to do with a limit of $75 for laboratory and diagnostic fees prior to hospitalization, provided the patient is subsequently hospitalized for that condition, and $50 for tests and procedures after hospitalization.

A fourth possible exception to hospitalized benefits is radiation therapy if it is begun while the patient is hospitalized and continued after hospitalization.

There have been very few instances in Kansas but some in other states where physicians have charged a Medicare patient fees in addition to those received from the government. Such procedure is strictly contrary to the contract under which the Medicare program operates. The practicing physician is not obligated to accept a Medicare patient, but if he submits a bill to Medicare he must also check A or B under Item 29 of Claim Form 1863 and must list the true situation under Item 26. For the exceptions listed above, that item may show $15 for other than hospitalized care in obstetrics or accidents. The government, however, considers Medicare to be a full coverage program within the limits of the conditions that are covered and guarantees to its patients that there will be no additional medical charge.

A considerable number of claims, 70 to be exact, have been delayed in processing. Those were the claims that could not immediately be justified by the fee schedule, and they were submitted to the Medicare Committee. This committee has met three times for all-day sessions considering the claims that have been submitted. Some have had to be rejected because they could not qualify under Medicare. In those instances the patient becomes responsible for payment of the bill. In others, the claim was still further delayed because it had to be sent to Washington for a ruling. In still others, the amount of charges was reduced by the committee because, for one reason or another, the physician's fee and that in the established fee schedule did not agree. Those three categories will reduce in number as rapidly as physicians become acquainted with the program.

There is one other category in which claims always will be delayed, and that is where unusual care is required for circumstances not covered in the fee schedule. Those situations are covered by individual consideration, and each claim, after reaching the Blue Shield office, is sent to the Medicare Committee and then to Washington before it may be processed.

It is the hope of the committee that Kansas doctors will continue to cooperate with the plan, and there have been very few problems of any importance whatever with reference to this program.

Twenty Questions

Editor's Note. Reproduced below is a column written by Peter Edson, NEA Staff Writer, on May 31. It is being printed here with permission of NEA Service, Inc.

Retiring Treasury Secretary George M. Humphrey has devised a new game of "20 Questions" to find out if there is anybody around who is a real, true advocate of government economy.

This game can be played any place you get a group of people together—at a woman's club, a chamber of commerce, any knife-and-fork club luncheon gathering, in a labor union or farm organization meeting, or at a cocktail party.

The rules are simple. Let the chairman ask all those present to stand. The chairman then proceeds to read off the 20 questions given below. Telling the

truth and nothing but the truth, every person who answers an honest, "Yes!" to any of the questions must sit down. Such person is counted out as not being a true believer in government economy.

STANDEE IS "IT."

Then repeat this process for every question in the list. If there is anyone still on his or her feet at the end, that person is "it"—a real devotee of decreased government spending.

All set? Here's the first question:

1. Have you ever opposed raising U. S. postage rates so as to make the U. S. Post Office Department self-supporting?

If you answer, "Yes!" sit down. You're out. Next:

2. Have you supported programs for greater federal expenditures in your community for housing or slum clearance?

3. Have you ever wanted the government to do a free dredging or flood control project on some nearby waterway?

4. Have you ever wanted Congress to pass a "pork barrel" appropriation for some dam or reclamation project?

DORM FOR YOUR COLLEGE?

5. Have you ever wanted the government to help build a new dormitory for your favorite college?

6. Have you favored more federal funds for community development, such as sewage disposal or water supply projects?

7. Have you favored federal ship building subsidies for the maintenance of an American flag merchant marine?

8. Have you favored high, rigid price support subsidies on American farm products?

9. Have you wanted the government to continue subsidizing uneconomic mining operations by guaranteed rates of payment?

10. Have you ever advocated greater expenditures for a long list of "welfare" activities—including school lunches, medical research, aid to education and so forth?

11. Have you ever been associated with groups seeking Hill-Burton act funds for a new hospital in your area?

EVER PROTEST?

12. Have you ever protested when the Army, Navy, Air Force or Veterans Administration proposed closing or consolidating a government hospital in your area, for reasons of economy?

13. Have you ever indorsed increasing pensions or hospitalization benefits for veterans whose disabilities are NOT connected with military service?

14. Have you ever wanted the government to provide your community with a new airport?

15. Has any company with which you are connected ever received any benefits from accelerated tax amortization allowances?

16. Have you ever protested when the government proposed closing up some military installation or ending some business-type activity which would have taken a government payroll out of your community?

17. Have you supported greater federal appropriations for Rural Electrification Administration, Tennessee Valley Authority or any other public power projects?

GRANTS-IN-AID?

18. Have you favored federal grants-in-aid to the states for highway construction, drought relief, disaster loans, aid to depressed areas, public assistance for combating juvenile delinquency?

19. Have you ever urged greater federal expenditures for recreational facilities in the national parks, national forests or for the fish and wildlife service?

20. Have you ever written your Congressman to help you get a job, a government contract or for tax relief or some other special favor that would cost Uncle Sam some money?

Anybody still standing, who answered, "No!" to all those questions? If so, give him the prize.

World Medical Association

A resolution approving the World Medical Association was passed by the House of Delegates of the American Medical Association at its June meeting in New York City. Membership fee in the international organization is $10 per year, which includes a subscription to the quarterly publication, *World Medical Association Journal*. Dues may be paid to World Medical Association, 10 Columbus Circle, New York 19, New York. The A.M.A. resolution follows:

Whereas, The World Medical Association is the only international medical organization representing the practicing profession in the fields of medical economics and medical education and devoted to protection of the freedom of the practice of medicine; and

Whereas, The United States Committee of W.M.A. was organized in 1948 to enable all American physicians to render support to the objectives of The World Medical Association and help improve the status of organized medicine internationally; and

Whereas, After nine years only 5,000 U. S. physicians have become members of the U. S. Committee,

although both the Association and the Committee are engaged in projects of vital interest to every American physician; and

Whereas, The House of Delegates of the A.M.A. at its Clinical Session in November 1956 declared: "It is difficult . . . to believe that any physician in the United States . . . is not a member of the (U. S. Committee) W.M.A. . . . Further expansion of the U. S. Committee will be necessary if the American viewpoint is to be continually and effectively presented by our spokesmen in The World Medical Association and, through them before other international bodies, to protect the interest and aims of medicine. . . . Surely physicians will wish to share in this international effort"; therefore be it

Resolved, That the House of Delegates of the American Medical Association reiterate its support of The World Medical Association and recommend that every member of the American Medical Association join the U. S. Committee of The World Medical Association; and be it further

Resolved, That the component state associations be urged to support and give official recognition to the state chairmen and subcommittees of the U. S. Committee in order to achieve the objectives of The World Medical Association in protecting the freedom of medical practice and increasing the influence of the practicing medical profession at the international level.

Medical Meeting at Norton

All members of the Kansas Medical Society are invited to attend a scientific and social meeting to be held at the State Sanatorium for Tuberculosis at Norton the afternoon and evening of October 6, under sponsorship of the sanatorium and the Northwest Kansas Medical Society. The program will begin at two o'clock.

Two speakers will discuss histoplasmosis and show slides, Lt. Col. Richard R. Taylor, chief of research and development, Fitzsimons Army Hospital, Denver, and Dr. L. M. Furcolow, medical director, U. S. Public Health Service, Kansas City. After an intermission Dr. Roger Mitchell, director of the Colorado Foundation for Research in Tuberculosis, Denver, will speak on "Emphysema as an Ever Increasing Clinical Problem," and Dr. John L. Morgan, Emporia, will discuss "Clinical Aspects of Chronic Cor Pulmonale."

A social hour at the home of Dr. C. F. Taylor, superintendent of the sanatorium, will be followed by a banquet at the Lathrop Building. The evening event will be a "Stump the Expert" program with case histories presented by those attending. Wives of physicians who attend the meeting will be entertained at the Taylor home. Advance reservations are suggested.

Clinical Conference in Oklahoma City

The Oklahoma City Clinical Society will open its 27th annual three-day conference at the Biltmore Hotel, October 28. Lectures and discussions will be presented by 15 guest speakers from medical and teaching centers throughout the nation. There will also be specialty lectures, a clinicopathological conference, and daily luncheon roundtable question and answer sessions.

Social events will include a banquet on Monday evening with Kenneth McFarland, Ph.D., Topeka, as speaker, specialty group dinners on Tuesday evening, and a dinner dance on Wednesday evening.

The conference has been approved for credit by the American Academy of General Practice. All physicians who are members of their county societies are invited.

Board Elects Officers

William P. Callahan, M.D., Wichita, was named president of the new Kansas Healing Arts Board at a meeting in Kansas City on August 6. Another member of the Kansas Medical Society, Francis J. Nash, M.D., Kansas City, was chosen to serve as secretary. Richard Gibson, D.O., Winfield, was elected vice-president. The board is made up of five doctors of medicine, three osteopaths, and three chiropractors.

Symposium on Asian Influenza

A feature of the conference of the Kansas City Southwest Clinical Society, to be held in Kansas City, September 30 through October 3, will be a symposium on Asian influenza at a luncheon session on the opening day. Four speakers will present papers, after which there will be a question and answer period.

The program will include: "Origin and Spread of Asian Influenza," Dr. William H. Stewart, United States Public Health Service, Washington; "Status of Vaccine Research and Immunological Problems," Dr. Tom D. Y. Chin, Public Health Service Communicable Disease Station, University of Kansas Medical Center; "Organizational and Mobilization Plans in Case of an Epidemic," Dr. H. M. Hardwicke, Jefferson City, and "Treatment of Asian Influenza and Management of Complications," Dr. Harold C. Lueth, chairman of A.M.A. committee to combat Asian influenza, Chicago.

Clinicopathological Conference

Pulmonary Lesions, Hypercholesterolemia, Hepatomegaly, Jaundice and Coma in a Young Man

Case Presentation

We are concerned today with a 20-year-old Negro man who entered the University of Kansas Medical Center for the third time on September 13, 1956, and who died on September 15, 1956.

He was first admitted to this hospital on June 16, 1956. He had felt well until April, 1956, when he first noted a feeling of fullness in his abdomen after meals. Since that time he had lost 25 pounds and had noticed a mass (which was more marked postprandially) in the right lower quadrant of the abdomen. He had had no melena, hemoptysis, hematemesis, diarrhea, acholic stools, dark urine, fatty food intolerance, fever, chills, cough, perspiration, or shortness of breath.

In May, 1956, his physician told him that he had an enlarged liver and "spots" on his lung.

His past history and system review were non-contributory. Both parents and two siblings were living and well.

The patient was a thin, chronically ill, colored man who appeared to be in no acute distress and who was alert and cooperative. His blood pressure was 170/130; the pulse rate 104; respiratory rate, 24; temperature, 100. Examination of the optic fundi revealed numerous areas of white edema residues about the discs, particularly in the macular area. There were also numerous areas of superficial flame-shaped hemorrhage and arteriovenous crossing defects. The tongue was red and coated. There was no cervical adenopathy. The chest was clear to percussion and auscultation. The heart was not enlarged; the second aortic sound was greater than the second pulmonic sound. One observer described a pleuro-pericardial friction rub over the precordium which was obliterated by inspiration, and another described a grade III precordial systolic murmur. The liver was extremely large and nodular and extended to the iliac crest. The spleen was palpable 4 cm. below the left costal margin. There was no fluid wave and no adenopathy. The remainder of the examination was within normal limits.

The specific gravity of the urine was 1.012 with a faint trace of albumin and 2 to 4 pus cells per high power field. The red count on admission was 4,950,000 with 15.3 gm. hemoglobin; the white count was 4,700 with 70 per cent polymorphonuclears, 19 per cent lymphocytes, 1 per cent eosinophils, 2 per cent basophils and 8 per cent monocytes. Subsequent blood counts showed a gradual drop of the hemoglobin to 9.3 gm. with 3,340,000 red blood cells at the time of discharge on July 9, 1956, but the white count was essentially unchanged. The platelet count remained approximately 500,000 throughout his hospitalization. The VDRL was nonreactive.

The serum calcium was 5.9 mEq/L; phosphate, 1.3 mEq; sodium, 139 mEq; potassium, 4.6 mEq; carbon dioxide, 30.6 mEq; chlorides, 94 mEq. The blood sugar was 68 mg. per cent; the serum cholesterol was 1,034 mg. per cent with 52 per cent esters; the blood urea nitrogen was 8.0 mg. per cent on admission and 20.5 mg. per cent on discharge. The serum iron was 78 gamma per cent; prothrombin time, 75 per cent of normal; bleeding time, 1.5 minutes; clotting time, 22 minutes. The urine 17 ketosteroids was 2.5 mg. per 24-hour period. The urinary catecholamines were not increased, and a phentolamine (regitine) test was negative. The blood ammonia was 143 gamma per cent; serum transaminase, 172 GOT units. The blood sedimentation rate was 17 mm. in one hour. Numerous target cells were seen on peripheral blood smear. A hepatogram revealed a direct serum bilirubin of .4 mg. per cent with a total bilirubin of 2.7 mg. per cent; alkaline phosphatase, 6.5 millimoles; cephalin cholesterol, negative; thymol turbidity, 5 units; serum albumin, 5.36 gm. per cent; and serum globulin, 2.89 gm. per cent. Cytologic examinations of the urine revealed numerous clumps of malignant cells (class V) on two occasions.

During the first hospitalization his blood pressure ranged from 160/100 to 190/120. A liver biopsy was done on June 25, 1956. He had several episodes of epistaxis. A trial course of x-ray therapy to the abdomen was given before his discharge, and, as an outpatient, he received a total of 400 roentgens depth dose through the anterior and posterior abdominal portals. He was dismissed, to be followed in the outpatient clinic, on July 9, 1956.

On August 22, 1956, he had a hemorrhage in the

Edited by Jesse D. Rising, M.D., and Mahlon Delp, M.D., from recordings of the conference participated in by the departments of medicine, pediatrics, surgery, radiology, and pathology of the University of Kansas Medical Center as well as by the third and fourth year classes of medical students.

left lower gingival area which continued until the day of his second admission on August 25.

The patient was quiet, depressed, and expectorating moderate amounts of bloody mucous material. His blood pressure was 120/80; pulse, 120; respiration, 18; temperature, 98.6 degrees. There was radiation pigmentation over the skin of the abdomen. Small pustules were seen on the mid-chest and on the right side of the nose. There was no peripheral adenopathy. The funduscopic examination revealed narrow arterioles and many exudates. The chest was clear to percussion and auscultation. The liver was firm and palpable below the right iliac crest. There was bleeding between the second and third left lower molars.

The urinalysis revealed a specific gravity of 1.020 with negative albumin and sugar. There were rare pus casts, red cells, and leukocytes. The red count was 3,080,000 with 9.3 gm. of hemoglobin; the white count was 3,400 with 59 per cent polymorphonuclears, 15 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils, and 22 per cent monocytes. An occasional atypical lymphocyte was seen. There was moderate anisocytosis and macrocytosis with slight to moderate poikilocytes and fragmentation of the red blood cells. There was considerable variation in color of the erythrocytes. The platelet count was 176,000 per cubic millimeter. The hematocrit was 29.5 ml. per 100 ml. of blood. The mean corpuscular volume was 96 cu. microns; the mean corpuscular hemoglobin, 29.2 micrograms; mean corpuscular hemoglobin concentration, 31.2 per cent. The bleeding time was one minute; coagulation time, 20.5 minutes; clot retraction was complete in 45 minutes. The prothrombin time was 70 per cent of normal. There was no lysis of the incubated clot.

Attempts were made to stop the bleeding with local pressure, Gelfoam packs, epinephrine packs, astringent mouthwash, intravenous conjugated estrogenic substances (Premarin), intramuscular Adrenosem, intravenous and intramuscular koagamin, and intramuscular posterior pituitary extract. All of these methods failed. The patient was given 500 ml. of whole blood on August 25, and on the morning of August 26 the bleeding stopped spontaneously, but he was given an additional 500 ml. of whole blood at this time. He was discharged on August 29 with a red count of 3,110,000 and 9.9 gm. of hemoglobin. There was no bleeding at that time.

Following his dismissal his condition became steadily worse and was marked by progressive lethargy, anorexia, jaundice, and incontinence of urine and feces. He was admitted for the third time on September 13, a thin, jaundiced, stuporous, terminally ill man. The blood pressure was 130/80; the pulse was 90 and regular; respiration, 24. The skin was jaundiced and appeared dehydrated. There was no adenopathy. The neck was supple. The fundi showed numerous exudates, and the sclerae were icteric. There was dullness to percussion in the right base with bronchial breath sounds heard over that area. The second aortic sound was greater than the second pulmonic sound. There was a grade II blowing systolic murmur at the pulmonic area which was transmitted over the precordium. The radiation pigmentation was still present over his abdomen. The liver was hard, nodular, and palpable below the iliac crest. The spleen and kidneys were not palpable. The peripheral pulses were good bilaterally. There was a coarse tremor of the hands, otherwise the neurological examination was normal with the exception of the deep stupor.

The urine had a specific gravity of 1.014 with 1 plus albumin, negative sugar, and positive hematest. It was loaded with motile bacteria and contained 8 to 10 pus cells per high power field. The red blood count was 2,300,000 with 7.5 gm. hemoglobin; the white count was 12,640 with 77 per cent polymorphonuclears, 65 per cent filamented, 12 per cent nonfilamented, 18 per cent lymphocytes, 3 per cent eosinophils, and 3 per cent metamyelocytes. There were 17 nucleated red blood cells per 100 white blood cells. The non-protein nitrogen was 59.5 mg. per cent; blood urea nitrogen, 37 mg. per cent; blood sugar, 107 mg. per cent; serum sodium, 138 mEq/L; potassium, 4.4 mEq; carbon dioxide, 14.2 mEq; chlorides, 96 mEq; blood ammonia, 297 gamma per cent; transaminase, 11 GOT units per milliliter. A hepatogram revealed alkaline phosphatase 5.1 millimol units; direct serum bilirubin, 20.6 mg. per cent; total bilirubin, 32.5 mg. per cent; cephalin cholesterol, 1 plus; thymol turbidity, 24 units; serum albumin, 3.41 gm. per cent; serum globulin, 2.69 gm. per cent; serum cholesterol, 472 mg. per cent with 12 per cent esters.

The patient was admitted primarily for terminal care. Medication consisted of intravenous fluids for dehydration and sponge baths to reduce his fever. On September 14 he was given 40 gm. of monosodium glutamate, but there was no increase in his responsiveness. He also received intravenous tetracycline and corticotropin, and oxygen by nasal catheter. He became progressively worse, and his blood pressure, terminally, was 100/60 with a pulse rate of 94. He was afebrile at the time of death, and he died quietly.

Dr. Mahlon Delp (moderator): Are there any questions of Dr. Dunn?

Edward L. Johnson (fourth year medical stu-

dent)*: Was there any previous history of jaundice?

Dr. Marvin Dunn (resident in medicine): No.

Mr. Johnson: Was there a history of poor dietary habits or alcohol?

Dr. Dunn: He had a normal dietary history, and there was no history of alcoholism.

William Harrin (fourth year medical student): Were there any skin lesions on the parents or siblings?

Dr. Dunn: No.

Richard E. Heikes (fourth year medical student): Could you describe the liver more fully?

Dr. Dunn: The liver was firm, massive, and nodular.

Alexander Krantz (fourth year medical student): Were the testicles descended, and were they atrophied?

Dr. Dunn: The testicles were descended, and no atrophy was found.

Otis O. Moseley (fourth year medical student): What was the urinary output in the hospital?

Dr. Dunn: It was low during his last admission.

Mr. Krantz: What was the result of the liver biopsy?

Dr. Dunn: The cells showed undifferentiated malignancy.

Mr. Johnson: What were the results of the trial course of x-ray?

Dr. Dunn: The liver became somewhat smaller.

Mr. Moseley: Were lipid determinations done?

Dr. Dunn: No.

Mr. Heikes: Had he had any moles?

Dr. Dunn: No.

Mr. Harrin: Was his urine dark during any of his hospitalizations?

Dr. Dunn: No.

Mr. Moseley: Was there any history of hypertension?

Dr. Dunn: No.

Mr. Johnson: Were the femoral pulses palpated?

Dr. Dunn: Yes, they were equal bilaterally.

Mr. Krantz: Was there previous history of a heart murmur?

Dr. Dunn: No.

Mr. Moseley: Was there any occult blood in the stools?

Dr. Dunn: No.

Mr. Johnson: Was a Coomb's test done on the first admission?

Dr. Dunn: No.

Mr. Harrin: Were bilirubins done on his second admission, and was he clinically jaundiced?

Dr. Dunn: He was not jaundiced and no bilirubin determinations were done.

Dr. Delp: We will now see the electrocardiograms.

Mr. Harrin: The electrocardiogram made on June 18, 1956, shows some decreased voltage in the chest leads (Figure 1). I interpret this tracing as a left axis deviation compatible with left heart hypertrophy.

Dr. Delp: Do you have any comment, Dr. Lin?

Dr. T. K. Lin (cardiologist): I would not make the diagnosis of left heart hypertrophy from this tracing.

* Though a medical student in May, 1957, when this conference occurred, he, like the others referred to as students, received the M.D. degree in June, 1957.

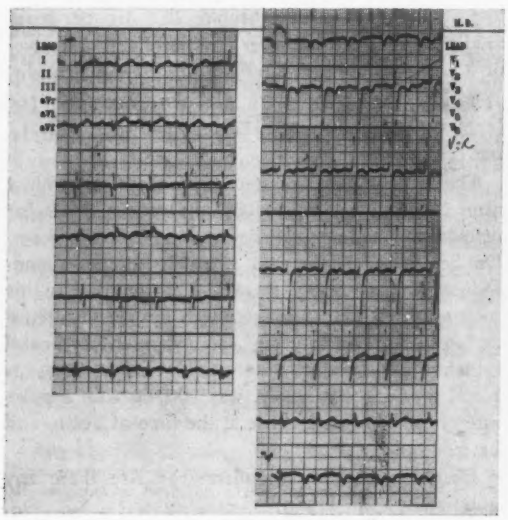


Figure 1. Electrocardiogram made on first admission.

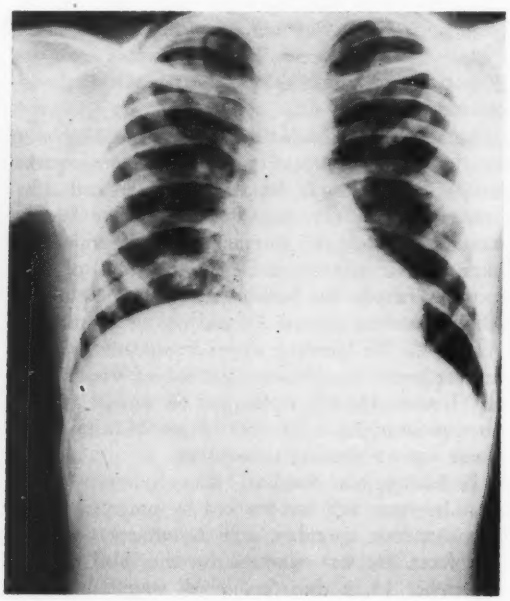


Figure 2. Chest x-ray taken during first admission.

Dr. Delp: May we have x-rays, please.

Doris M. Kells (fourth year medical student): The chest x-ray taken during the first admission shows circumscribed patches of soft tissue infiltration throughout all lung fields (Figure 2). There are no bony abnormalities, and the costophrenic angles are clear. The heart is not remarkable. The right diaphragm is elevated. This film is compatible with metastatic lesions of the lungs and with hepatomegaly.

No bony abnormalities are seen on the kidney-ureter-bladder film, but there is diffuse haziness extending down from the diaphragm to close to the iliac crest. I interpret this as being a massive liver.

The intravenous pyelogram shows good concentration of the dye bilaterally. There are no abnormalities of the calyces, pelves, or ureters, and the bladder is smooth. The left kidney is lower than the right, a reversal of the usual position.

The upper gastrointestinal films show a diffuse haziness on the right, with displacement of the stomach and small bowel to the left. There is no evidence of intrinsic disease of the stomach or intestine. The lower gastrointestinal film shows that the colon is displaced downward with no intrinsic abnormalities noted.

The film of the lung, taken on the last admission, shows greater soft tissue infiltration and greater elevation of the right diaphragm than the previous chest film (Figure 3). The degree of soft tissue infiltration makes it impossible to evaluate the costophrenic angles. The heart is not remarkable. I consider this film consistent with growth of the metastatic lesions and a greater enlargement of the liver in comparison with the previous x-ray.

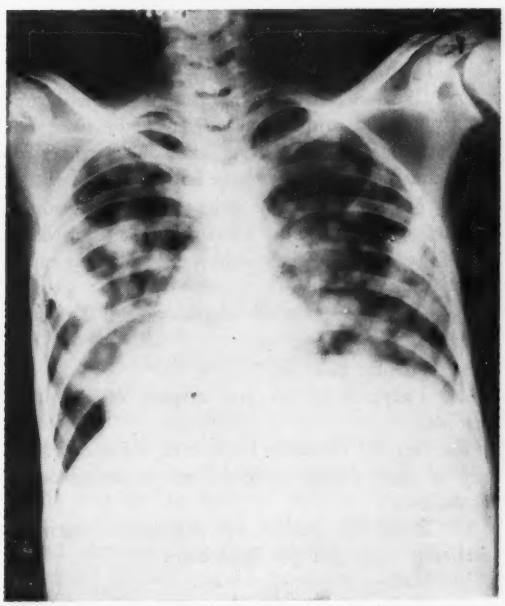


Figure 3. X-ray of lung taken during last admission.

In summary, I interpret this series of x-ray films as being compatible with metastatic involvement of the lungs and with hepatomegaly. It should be noted that no primary malignant sites other than the liver have been demonstrated in these films.

Dr. Delp: Thank you. We will now have the differential diagnosis.

Differential Diagnosis

Mr. Heikes: Although a malignant tumor is rather unusual in this age group, the diagnosis of some type of malignancy seems obvious from a brief summary of the case. There was a 25-pound weight loss in two months and a history of consulting another physician who told him he had a large liver and "spots" on the lung. Physical findings revealed an emaciated male with a huge, firm, nodular liver. The x-rays showed metastases in the lungs. Cytologic studies of the urine showed grade V cells on two occasions. There was a progressive decrease in hemoglobin, and the hepatogram was consistent with neoplastic disease of the liver, especially the elevated transaminase and blood ammonia. In the hospital the patient rapidly became worse, and he died in three months. The terminal liver function tests indicated severe liver damage, and he developed a tremor, became stuporous, and, finally, comatose before death.

I will first consider primary tumors of the liver. Approximately one per cent of malignancies coming to autopsy are primary carcinoma of the liver. This disease is most common in the sixth decade with a small peak of incidence in the first two years of life. Most patients with carcinoma of the liver have some definite predisposing factor, and it is important to consider whether this patient did. In hemochromatosis 10 per cent of the cases develop carcinoma of the liver, but we have no evidence of diabetes, increased pigmentation of the skin, heart failure, or elevated serum iron in this patient. Parasitic infections of the liver also predispose to primary carcinoma, but there is no evidence for such an infection. In this country cirrhosis is a most important predisposing factor. Three to four per cent of cirrhotic patients develop primary carcinoma of the liver as compared with 0.05 per cent of non-cirrhotic patients.

There are two types of primary carcinoma of the liver. About 80 per cent are hepatoma, and 90 per cent of these are superimposed on a pre-existing cirrhosis. The remaining 20 per cent are cholangioma, and only 50 per cent of these cases have pre-existing cirrhosis.

In this patient I can rule out portal cirrhosis because there is no history of alcoholism, nutritional deficiency, dark urine, clay-colored stools, or ascites; and the laboratory findings are not compatible with that disease.

There are two types of biliary cirrhosis. For the primary type we need a history of malaise of long duration, pruritus, early jaundice, large liver, xanthomata, and attacks of pain simulating cholecystitis. This disease is more common in women. Laboratory findings of low thymol turbidity, negative cephalin cholesterol, extremely high cholesterol, and elevated bilirubin are all consistent with this disease, but one would expect a higher alkaline phosphatase. I cannot rule out this diagnosis, but I consider it unlikely.

The secondary type can be dismissed quickly because there is no evidence of extra-hepatic obstruction. The fact that no good evidence for any predisposing factor can be found militates against the diagnosis of a primary tumor of the liver; furthermore, patients with primary carcinoma of the liver commonly have a strongly positive cephalin cholesterol, whereas patients with metastatic disease of the liver do not.

I will, therefore, now consider some neoplasms that metastasize to the liver and might produce some of the findings present in this protocol. Pheochromocytoma is most common in young and middle-aged groups. Eight per cent of these tumors are malignant, but the metastases are not massive. I can rule out this tumor on the basis of negative phentolamine and catecholamine tests.

Discussion of carcinoid tumor has been popular in many medical journals recently. In its metastatic form it is a rare tumor, but it does occur at any age. It is usually slow growing, but at times it may become quite malignant and produce a large liver. Flushing, cyanosis, diarrhea, abdominal cramps, and wheezing are usually present when it involves the liver. A pulmonic systolic murmur and elevated blood pressure may accompany these symptoms.

Renal cell carcinoma usually occurs in persons over 50 years of age, and it is rare under the age of 30. It predominates in males over females in a 3:1 ratio. It is not unusual for a small primary tumor to give rise to multiple and massive metastases, but a number of cases have been reported in which metastases caused a large liver, some being over 5,000 gm. Of the fatal cases, three-fourths metastasize to the lung and one-fourth to the liver. The grade V cells in the urine sediment favor this diagnosis, but there was not the degree of hematuria which one expects in about 80 per cent of all renal cell carcinomas.

The last type of tumor I shall consider is the malignant melanoma. This, too, is a rare tumor having only a 0.7 per cent incidence in one series of 1,200 cancer autopsies. It occurs at any age, but three-fourths of the cases occur between 30 and 70 years of age. This neoplasm frequently has a bizarre behavior. Multiple and massive metastases can arise from a benign looking mole, and at times no primary site is demonstrable. Primary tumors are found in tissues other than the skin, the ciliary body and choroid of the eye being rather common sites. They may also be found in the mucous membrane and the adrenal cortex. Of the various metastatic lesions that cause huge livers, this tumor is the most frequent offender.

In summary, I believe pheochromocytoma and carcinoid tumors can be ruled out. Primary liver carcinoma and renal cell carcinoma are good possibilities, but I think malignant melanoma is the best diagnosis. I suspect that the primary site was in the eye (as that is the most frequent site for a hidden primary), or that no primary could be found. This patient had massive liver metastases which caused severe liver failure, as evidenced by the abnormal liver function tests, jaundice, stupor, tremor, coma, and finally death.

Clinical Discussion

Dr. Delp: What is your diagnosis, Mr. Krantz?

Mr. Krantz: Renal cell carcinoma.

Dr. Delp: Mr. Johnson?

Mr. Johnson: Renal cell carcinoma.

Dr. Delp: Miss Kells?

Miss Kells: Malignant melanoma, but I cannot rule out a hepatoma.

Dr. Delp: Mr. Moseley?

Mr. Moseley: Primary tumor of the liver.

Mr. Harrin: Renal cell carcinoma.

Dr. Delp: You mentioned some of the factors predisposing to primary carcinoma of the liver, one of which was cirrhosis. What kind of a cirrhosis do you think this man might have had?

Mr. Krantz: Probably primary biliary cirrhosis because of the markedly elevated cholesterol, but I would expect to see a much higher alkaline phosphatase.

Dr. Delp: You do not think he had Laennec's cirrhosis?

Mr. Krantz: No, sir.

Dr. Delp: Why do you dispose of Laennec's cirrhosis?

Mr. Krantz: Primarily because of his age and history of good dietary intake. There is no history of alcoholism.

Dr. Delp: Mr. Heikes, you disposed of Laennec's cirrhosis; what did you substitute?

Mr. Heikes: Biliary cirrhosis.

Dr. Delp: Mr. Krantz, how did you explain the

elevated blood cholesterol? On the basis of biliary cirrhosis?

Mr. Krantz: Tannhauser[3] lists two major groups with increased serum cholesterol. These can be differentiated by whether the patient has a clear or chylous serum. This patient had a clear serum, and we can divide the causes of hypercholesterolemia with a clear serum into three groups: familial xanthomatous hypercholesterolemia, xanthomatous biliary cirrhosis, or hypothyroidism. Hypothyroidism can quickly be ruled out in this case. I think xanthomatous biliary cirrhosis is the best diagnosis on the basis of the material presented to us. Xanthomatous biliary cirrhosis is a primary liver disease with inflammation of the small cholangioles which subsequently close up, and cause a reflux of cholesterol, bilirubin, and alkaline phosphatase. In addition, the liver apparently has an increased secretion of cholesterol in this disease which contributes to the remarkably elevated cholesterol. At times the bilirubin is quite low and the cholesterol is quite high, which is difficult to explain. It is essentially a benign disease, and patients usually live for a long time. I believe the patient had this disease, and that it rapidly degenerated into a malignant hepatoma.

Dr. Delp: Mr. Johnson, the patient came in with a blood pressure of 170/130. How do you explain the hypertension?

Mr. Johnson: I explain that on the basis of renal ischemia. According to Goldblatt there can be pressure on the renal parenchyma and on the renal artery from an enlarged liver; there can also be metastases into the lymph nodes occluding the renal arteries, and this in turn causes the abnormal kidney which is postulated to release renin which, when activated in the plasma, produces angiotonin, the agent responsible for the hypertension.

Dr. Delp: How do you explain the class V cells in the urine if this patient had a malignant melanoma?

Mr. Johnson: In Virchow's Archives of 1873 there is a report of a case of malignant melanoma with widespread metastases in which microscopic sections of the kidney showed a diffuse spread of malignant cells in the glomeruli and tubules.

Dr. Delp: Miss Kells, what is your explanation for the murmur?

Miss Kells: It may have been due to pulmonary stenosis. I assume that the murmur was heard before he had his profound anemia; therefore, I cannot explain this on the basis of anemia. Because it was recorded as being heard in the pulmonic area on the third admission, I believe it may have been due to pulmonic stenosis and congenital heart disease. I have no other explanation for it.

Dr. Delp: Now, a few comments from Dr. Berry.

Dr. Maxwell G. Berry (internist): It seems to me that there are a lot of incompatibilities which are difficult to tie together. The first is the age of the patient with a very malignant tumor; the second, an exceedingly high blood pressure; third, the hypercholesterolemia; fourth, the fact that he had an enlarged spleen when he came in here; and fifth, the nodular pulmonary metastases. It is difficult to account for all of these with one diagnosis.

As usual, I have to agree with the students and their original diagnosis of malignant melanoma, but it seems to me that we must assume that this man had obstruction to his biliary tract and to the venous return from the spleen, as well as some interference with renal circulation. I am not sure that I have ever seen obstruction of the renal vein cause hypertension. Malignant melanoma is one of the diagnoses that I made in reading over this protocol. I am hesitant to dismiss completely the diagnosis of some form of lymphoma because of the tendency to hemorrhage in this age group. Although nodules in the lung are rare in cases of this type, I still think that it is a possibility.

Dr. Delp: What is your explanation for the elevated cholesterol, Dr. Manning?

Dr. Robert Manning (resident in medicine): I think that it can best be explained on the basis of primary familial hypercholesterolemia or primary biliary cirrhosis.

Dr. Delp: Dr. Lin, would you venture an opinion on the murmurs that were described?

Dr. Lin: In the first place, one observer described a murmur while another observer heard a friction rub, both on the first admission. There was no murmur during the second admission, so I would assume that the first one must have been a friction rub. I doubt that the patient had congenital heart disease. The terminal murmur was probably due to anemia.

Dr. Delp: Do you think that the murmur could have been the hum heard over a cirrhotic liver?

Dr. Lin: That is a possibility, but it was quite high, being heard in the pulmonary area.

Dr. Delp: Dr. Kaul, what is your diagnosis?

Dr. Philip G. Kaul (internist): I think that this patient had primary biliary carcinoma superimposed on biliary cirrhosis.

Dr. Delp: Dr. Allbritten, do you have a diagnosis?

Dr. Frank F. Allbritten (surgeon): Primary carcinoma of the liver.

Dr. Delp: Dr. Bly, may we have your report?

Pathological Report

Dr. Chauncey G. Bly (pathologist): We too had trouble making only one major diagnosis, as you will

see. The patient was moderately jaundiced and severely emaciated; he weighed about 100 pounds, and he was six feet tall.

The liver, weighing 4600 gm., was filled with nodular tumor masses. So thoroughly distorted was the architecture that it was difficult to recognize grossly any remaining normal liver parenchyma. As is characteristic of many primary liver tumors, there was invasion of the main portal vein and its smaller branches; there was also invasion of the hepatic vein tributaries.

Microscopically, patches of many recognizable but distorted liver lobules showing both central veins and portal areas were seen between tumor nodules. These, together with other irregularly distributed, wide, multilobular bands of collapsed and increased fibrous tissue with few inflammatory cells, suggested that the liver represented post-collapse fibrosis or "post-necrotic cirrhosis" rather than biliary or pericholangiolitic cirrhosis remotely antedating the tumor. We would have been happier about this diagnosis of "post-necrotic cirrhosis" if there had been a previously known clinical episode of viral or chemical hepatitis. Moreover, some of the observed peri-lobular inflammation and the nodular regeneration of liver tissue were changes compatible with the regional "pericholangiolitic biliary cirrhosis" expected to follow local biliary obstruction and widespread destruction of liver tissue by tumor.

The small needle biopsy specimen taken three months before death was so completely filled with tumor that the state of the liver parenchyma and the amount of fibrous tissue present at that time could not be reliably estimated. We cannot, therefore, state incontrovertibly that this patient did have cirrhosis before the hepatoma began, but we believe that he did. Although at one time antecedent cirrhosis was felt to be a necessary precursor to hepatoma, many investigators in the last few years have reported increasing numbers of cases in which cirrhosis has not been present.[2, 4, 5] This has been particularly true of the parenchymal cell hepatocarcinoma occurring in children and young adults.

On the other hand, Higginson, among others, seems to feel that in the African Negro hepatitis and/or post-collapse (-necrotic) cirrhosis may be of particular premalignant significance by somehow sensitizing or predisposing to hepatocarcinogenesis.[2]

The many focal small areas of fatty change present in this liver were not unexpected, since the patient had progressive ischemia of the surviving liver tissues, resulting from gradual compression of parenchyma and blood vessels by tumor masses and thrombi. Moreover, he had generalized malnutrition. Inspissated bile plugs were seen in interlobular and larger bile ducts, canals of Hering, and peripheral intro-lobular canaliculi, most prominent near obstructing tumor nodules.

Microscopically, the tumor had an organoid appearance with discrete clumps of cells, sometimes appearing as columnar cells lined up around a central space, simulating acinar structures. This also appeared in the needle biopsy tissue three months before death, and had suggested carcinoid or paraganglionoma as primary tumor possibilities at that time. Numerous mitoses were seen in the proliferating tumor cells. Many of the tumor areas closely resembled parenchymal liver itself, even showing abortive canaliculi filled with inspissated bile.

Peculiar tumor giant cells, sometimes with multiple large nuclei, characteristic of hepatocellular carcinomas, were numerous in several areas. In addition to nodular masses of tumor invading sinusoids and compressing parenchyma, cords of tumor cells were seen invading walls and lumens of vessels and lymphatics, sometimes appearing to float as free tumor emboli (Figure 4). Because of this proclivity to enter and spread through vascular channels, some investigators feel that hepatomas spread almost simultaneously in all directions from the primary site, to explain the massive involvement often seen in the liver at death. It is true that localized solitary primary liver tumors are occasionally seen at autopsy or surgery, some of them apparently resectable. On the

Figure 4. Low power view of liver. Large vessel at upper left is filled with tumor mass extending from tributary to the right. Dense collapsed connective tissue separates and extends into liver lobules in lower right part of field.

other hand, in experimental animal liver tumors and in most human liver tumors, the multicentric origin of the tumors or multiple primaries, with similar or dissimilar microscopic appearance, is more generally accepted.

Over the diaphragmatic surface of the liver were fibrinous peritonitis, organizing fibrous adhesions, and some acute hemorrhagic necrosis in the liver as well as the long-standing atrophy of gradual or partial ischemia. These were again due to the tumor throughout the liver, rather than to the previous small course of irradiation.

As expected from the observed tumor invasion and embolization of hepatic vein tributaries, the lungs were studded with tumor metastases, 2 to 50 mm. in diameter. Some of these were brownish-yellow throughout, resembling liver nodules. Others were greenish-yellow or white, depending on their degree of differentiation and bile production. Many of the hilar lymph nodes were also filled with tumor nodules. Abortive canaliculi filled with inspissated bile plugs were seen microscopically in many of these metastatic nodules (Figure 5).

In many areas of the brain there were numerous enlarged, pale astrocytes which were almost pathognomonic of hepatic coma and were associated with this patient's increasing blood ammonia.

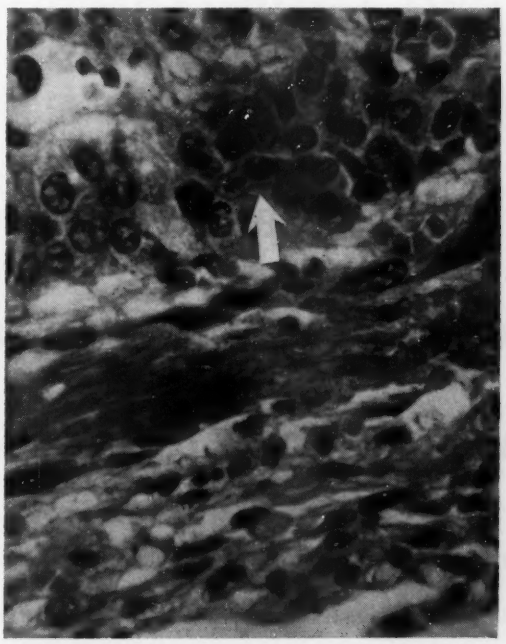


Figure 5. High power view of lung showing mass of liver tumor cells in upper half of field. The arrow points to a well-formed but abortive bile canaliculus filled with bile plugs.

The other main group of findings relate to this patient's severe hypercholesterolemia. He did not have extrahepatic biliary obstructions, skin or tendon lesions, or familial history. Nor do we have enough data to classify this finding except to call it "idiopathic hypercholesterolemia."[1] Grossly this seemed to be manifested by severe arterial atheromatosis, a greatly enlarged soapy-appearing spleen, weighing 500 gm., and peculiar, small, pale green foci in the bone marrow. Microscopically, large zones of pale, swollen, foamy cells were seen throughout the spleen, particularly beneath the capsule, surrounding central arterioles and around the trabeculae (Figure 6). Many foci were also seen in the bone marrow, liver, lung, lymph nodes, and pancreas. By the use of various stains and the polarizing microscope it was demonstrated that these cells contained not only cholesterol but also neutral fats and phospholipids. The spleen and marrow also showed hyperplasia of erythropoietic and myelopoietic cell series. There were several small foci of encephalomalacia, with a few phagocytes and lymphocytes. These seemed most likely to be micro-infarcts due to atherosis of cerebral arteries, although we do not have sections through specific occlusions.

The heart weighed 320 gm., which is slightly above the normal range for our patient's height and severe emaciation, and this is compatible with the brief history of hypertension. The two striking things about the heart and vessels were the distinct pallor

Figure 6. Medium power view of xanthomatous splenic follicle. The branching central arterioles in lower left field are surrounded by numerous, large, foamy cells.

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of fatty degeneration of the inner half of the myocardium attributed to ischemia, and the unusually numerous and soft atheromatous deposits around the aortic ring and involving the aorta, coronary arteries, and the larger visceral arteries, attributed to hypercholesterolemia. The renal arteries showed greatly thickened walls, and there were atheromata covering the intimal surfaces. This may conceivably explain the hypertension which was present up to the last two admissions.

There was no grossly visible evidence of scars or ischemic atrophy. Since the kidneys were of equal size, it is difficult to believe that there was any significant kinking of the right renal artery or compression of the kidney itself by the enlarged liver. There was no constricting perinephritis. Microscopically, there was nothing to relate to the hypertension; no arteriolar changes were seen anywhere. There was no evidence of primary or metastatic tumor in the kidney, and the misleading cytologic studies must, therefore, be filed under the category of false positives.

The probability that the damaged liver contributed (by its increasing inability to detoxify aldosterone and anti-diuretic hormone) to the patient's arterial hypertension, seems negated by the existence of normal blood pressure readings on his last two admissions when liver function was decreasing rapidly.

In regard to the relationship between the two main groups of lesions, (a) hypercholesterolemia, atheromatosis, and xanthomatosis; and (b) the cirrhosis and hepatoma: the serum cholesterol dropped steadily from over 1000 mg. per cent (52 per cent esters) three months before death to 472 mg. per cent (12 per cent esters) two days before death, and the liver biopsy showed numerous foamy xanthoma cells three months before death. These and the hyperalbuminemia three months before death indicated that the hypercholesterolemia antedated the hepatoma and liver damage. Moreover, the absence of fibrous tissue and inflammatory cells from the admittedly small needle biopsy specimen, the disproportionately low levels of alkaline phosphatase and direct-reading (one minute) serum bilirubin, and the absence of other evidence of obstructive biliary disease until very late, rule out the theory that this might have been the usual obstructive diffuse biliary cirrhosis or pericholangiolitic cirrhosis[3] with secondary hypercholesterolemia and hepatoma. Furthermore, it seemed most unlikely that the severe arterial atheromatosis and tissue xanthomatosis were produced during the last three months as the serum cholesterol levels fell. The sharp decline of esterification indicated that the serum cholesterol fell because of failure of liver function rather than because of tissue deposition of cholesterol.

In summary, I believe that this patient had two diseases: (a) idiopathic non-familial hypercholesterolemia with tissue xanthomatosis and atheromatosis; and (b) sub-clinical hepatitis and postnecrotic cirrhosis, subsequent well-differentiated juvenile type of hepatocarcinoma with biliary, vascular, and parenchymal invasion and compression, ischemia, pseudo- and complete infarcts of the liver, pulmonary metastases, liver failure, hepatic coma, and death. If, in deference to Dr. Berry's axiom earlier today on the number of allowable diseases, I had to put all of these together into one picture, I would unwillingly compound a series of improbabilities. These would be based on the as yet poorly substantiated concept that xanthomatosis of the liver can produce "hepatocellular hypercholesterolemic cirrhosis."[4] If this is true, hypercholesterolemia could then lead successively to xanthomatosis and cirrhosis, hepatoma, liver failure, and death.

Summary

Dr. Delp: Neither primary hypercholesterolemia nor primary carcinoma of the liver is a rare entity, but a combination of the two bearing a vague causal relationship to each other is unusual.

In retrospect the clinical impressions first voiced upon admission are still sound, i.e., hypernephroma with metastasis, melanoma with metastasis, and primary carcinoma of the liver. Failure to suggest hepatoma because of clear evidence of cirrhosis is not acceptable, because primary neoplasm is not uncommonly seen in children and young adults without previous existing cirrhosis. Correlation of the malignant liver lesion and the high blood cholesterol is expecting too much of the clinician.

Pathological Anatomical Diagnosis

Primary

Postnecrotic cirrhosis, moderate.

Primary carcinoma of the liver, hepatic cell type, with invasion of portal and hepatic veins, metastases to the lungs and the hilar lymph nodes, and extension to the anterior wall of the abdomen.

Incomplete and complete organizing infarcts of liver.

Bile thrombi in canaliculi of liver and small intrahepatic bile ducts with generalized juandice.

Hyperplasia of the bone marrow; foci of erythropoiesis of the spleen.

Recent and organizing localized fibrinous peritonitis of the subdiaphragmatic space and between liver and anterior wall of abdomen.

Proliferation of pale pleomorphic protoplasmic astrocytes of the brain.

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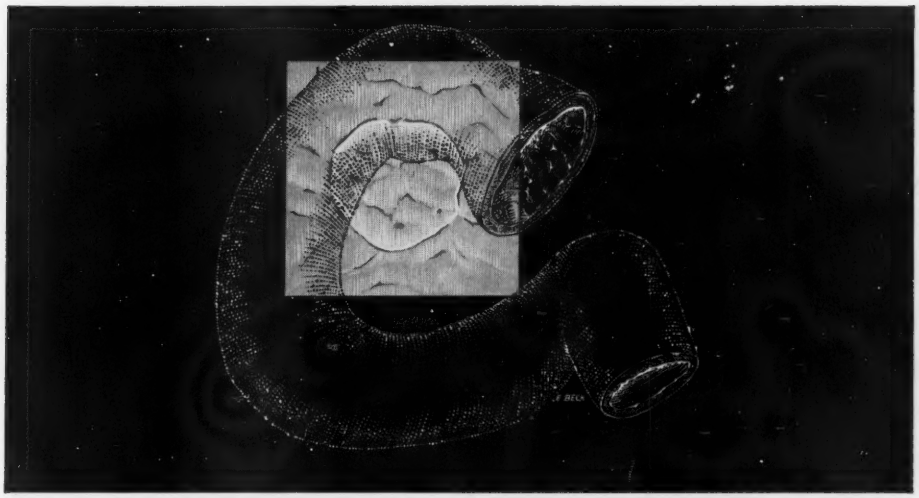

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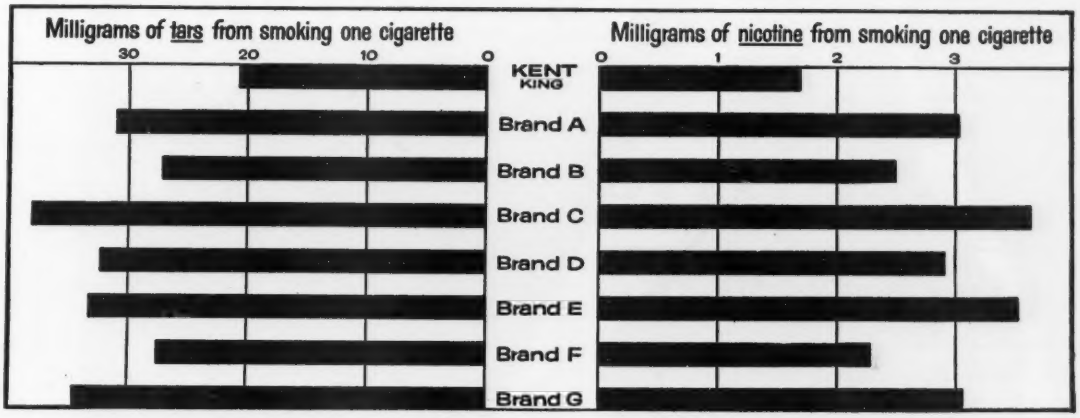

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Atherosclerosis of the aorta, coronary and renal arteries.

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PHYSICIANS' ACTIVITIES

Dr. Harry G. Gianakon, of the University of Kansas School of Medicine, is the author of a paper, "Psychiatric Aspects of Pain," published in the July issue of *The Journal-Lancet.*

A physician new in this state, **Dr. Wilmer A. Harms,** has announced the opening of an office in Hesston.

Dr. Henry C. Eichelmann, who has been practicing in Norwich since 1949, moved to Walton, New York, last month and is practicing there in association with three other physicians.

Color slides of a trip around the world with 16 other doctors were shown by **Dr. Willard J. Kiser,** Wichita, at a recent meeting of the Wichita Exchange Club.

Dr. Robert E. Delphia, a 1956 graduate of the University of Kansas School of Medicine, completed internship at St. Joseph Hospital, Kansas City, Missouri, in July and has begun practice in Olathe in association with **Dr. William McCann** and **Dr. Joseph Pierron.**

A paper by **Dr. E. Grey Dimond,** of the University of Kansas Medical Center, "The Generalist and the Internist," was published in the July 20 issue of the *Journal of the American Medical Association.*

Dr. Francis T. Collins, Topeka, and **Dr. Norton L. Francis,** Wichita, were among a group of physicians who attended the Boy Scout encampment at Valley Forge, Pennsylvania, last month.

A refresher course offered by the American Society of Anesthesiologists, Inc., at Los Angeles in October includes a paper by **Dr. Paul H. Lorhan,** of the University of Kansas Medical Center, "Geriatric Anesthesia."

Dr. Donald Wilcox, who has been practicing in Johnson County, has accepted appointment as acting director of the Kansas City-Wyandotte County Health Department.

A physician who has practiced in Hardtner for 21 years, **Dr. Hiroshi Yasuda,** has moved to Anthony and is practicing there in association with **Dr. H. L. Galloway.**

Dr. William Trekell, who recently completed a three-year residency in general surgery at the Staten Island Public Health Service Hospital, New York, has begun practice in Halstead at the Hertzler Clinic.

Dr. Kurt R. Reissman, associate professor of medicine at the University of Kansas School of Medicine, left August 1 to serve as visiting professor at the University of the Philippines College of Medicine at Manila. After eight months in the Philippines, he will visit scientific laboratories in England, Sweden, and Germany.

The American Board of Internal Medicine announces that **Dr. James C. Dowell,** Lawrence, has been certified as a diplomate.

Dr. Charles M. Poser, of the University of Kansas Medical Center, has been given the rank of assistant professor of neurology and will form a new section of experimental neurology within the department of medicine.

The United States Committee of the World Medical Association has announced the appointment of **Dr. L. S. Nelson, Sr.,** Salina, as chairman of the organization in Kansas.

Dr. Philip J. Antrim, who has been practicing in

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Russell since 1955, has moved to Attica and is now engaged in general practice there.

A feature story about **Dr. James G. Lee** was published in the August 15 issue of the *Eudora News,* in connection with a luncheon given in his honor by the Eastern Star on the occasion of his 89th birthday. Dr. Lee has been a member of the Eastern Star for a longer period of time than any other person in Kansas.

The Nelson Clinic, Manhattan, announces that **Dr. John McCrary** has joined its staff as a specialist in obstetrics and gynecology. Dr. McCrary, a graduate of the University of Nebraska College of Medicine in 1950, has been teaching at that institution in addition to carrying on a private practice.

Dr. Chauncey G. Bly, former associate professor of pathology and oncology at the University of Kansas School of Medicine, has become head of the department of pathology at Highland Hospital, Rochester, New York, and associate clinical professor of pathology at the University of Rochester School of Medicine.

Rural Health Meeting

How to develop more effective rural health programs will be the chief topic of concern at the American Medical Association's second study conference, October 4 and 5, for chairmen and members of state rural health committees. Sponsored by the Council on Rural Health, the conference will be held at Purdue University.

The opening session will be devoted to a discussion of organizational techniques of statewide rural health committees. Another session will feature representatives of leading farm organizations outlining their health programs. Following this latter presentation will be a discussion of ways that the medical profession and agricultural groups can best work together in developing better health programs. Registrants also will have an opportunity to get together with others from their own regions to discuss mutual problems.

Three New A.M.A. Exhibits

Three new exhibits previewed at the American Medical Association's 1957 Public Relations Institute in Chicago August 28-29 are now available for bookings by state and county medical societies.

(1) "Digestion"—shows the organs involved in digestion, the passage of food through the body, the mechanics of swallowing, the action of the stomach and intestines, and the body's absorption of food. (2) "Alcoholism Is Your Business"—(for professional audiences) gives the viewer an opportunity to eavesdrop on a conversation between a distraught spouse and the family physician over the treatment of alcoholism. (3) "Organs of the Human Body"—three dimensional models of the torso show location of various organs in the body and their functions.

Further information on these displays may be secured from the A.M.A. Bureau of Exhibits.

DEATH NOTICES

LEWIS A. CURRY, M.D.

Dr. L. A. Curry, 63, Topeka physician who specialized in obstetrics and gynecology, died on August 11 after an illness of two weeks. A graduate of Rush Medical College in 1922, Dr. Curry practiced first in Winchester, remaining there for 12 years. He later took postgraduate work at Tulane University and then practiced in Topeka for 25 years. He was a member of the Shawnee County Medical Society and of the Central Association of Obstetricians and Gynecologists.

CHARLES FRANCIS MCNAIR, M.D.

Dr. C. F. McNair, 79, an honorary member of the Reno County Medical Society since 1949, died at Hutchinson on August 9 after having been hospitalized for four months. A graduate of Kansas Medical College, Topeka, in 1905, he began practice in Castleton, then moved to Haven, and later to Hutchinson. During World War I he served in the Army as a captain in the Medical Corps.

JAMES LLOYD JENSON, M.D.

A coronary thrombosis suffered on July 28 by Dr. J. L. Jenson, Colby, who was vacationing in Colorado, caused his death at St. Joseph Hospital, Denver, on August 13. Dr. Jenson, 71, received his degree from Jefferson Medical College, Philadelphia, in 1912. He opened his office in Colby in 1930 and had been active in Northwest Kansas Medical Society affairs since that time. At the time of his death he was chief of staff of St. Thomas Hospital, Colby.

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Tears of the Poppy

A Review of the History of Opium

ARTHUR B. COLLOM, M.D., ***Eugene, Oregon***

With the flourish of modern medicinals, especially hordes of proprietary and synthetic preparations, we tend to forget the role of ancient herbal remedies in medicine. Some of these remedies have played a prominent part in medical therapy for over 2,000 years, forming the basis of modern therapeutics.

It is of interest to consider how herbs were adopted as medicines, and how, in some instances, this use persisted. Their first use was connected with religious and witchcraft healing rituals, and later the use of specific herbs as remedies must have been related to some unusual quality or characteristic as is shown by the following examples: the mountain ash, whose use was based on the beauty of its berries; the mistletoe, by remaining green after its host had become bare; the carminatives and antispasmodics, such as thyme and valerian, by their odor; the mandrake and foxglove, by their unique shapes; henbane and belladonna, by their toxic actions; and the poppy, both by the beauty of its flower and by its hypnotic powers.[16]

As late as the 17th century, the pharmacopoeias still contained long lists of herbs, though only a few had any real therapeutic value other than as placebos, and these few were usually adulterated and covered up by many worthless herbs in lengthy and complicated recipes. These many herbs persisted in use largely because their evolution had been unscientific without benefit of clinical experimentation and evaluation, and because the efficacy of a remedy was based, not so much on the type of ingredients, but on the quantity of ingredients it contained.

The whole aspect of ancient herbal remedies is interesting, but too broad for consideration in a paper of this type. For this reason I will use opium as a topic and trace its history from antiquity to modern times. Mention will be made of ancient records that probably indicate its first uses as a therapeutic agent. In some instances where a herbal remedy is referred to, the exact nature of which is not stated, I will include that reference to add interest. Then I will follow its course geographically and chronologically through the ages to modern time, using classical as well as scientific literature for reference.

We cannot know when the milky juice of the poppy capsule was first used for medicinal purposes, but from allusions to the poppy in antiquity we find that knowledge of its hypnotic power was discovered at an early date. Some translators of the famed Egyptian Eber's Papyrus, dated at near 1500 B.C., attribute the hieratic figure of a couch to opium and thus include opium in several of the contained recipes.*

The following are in Bryan's English translation of Joachim's work on the Eber's:[4] "Remedy which the goddess Isis prepared for the god Ra to drive out the pains that are in his head—berry of the coriander, berry of the poppy plant, wormwood, berry of the sames plant, berry of the juniper plant, honey. Make into one, mix with honey, and smear therewith in order to make him well forthwith. When this remedy is used by him against all illnesses in the head and all sufferings and evils of any sort, he will instantly become well."

"Remedy to stop the crying of a child—pods of the poppy plant, fly dirt which is on the wall. Make into one, strain, and take for four days. It acts at once!" The similarity of the ancients' method of stopping the child's crying over 3,000 years ago to the modern mother's remedy is remarkable.

Some Hebrew scholars claim a reference to poppy juice in the Old Testament of the Bible. The word rosh is used in connection with the word la'anah, or absinthe. Though rosh is translated as hemlock in the authorized version of the Bible, rosh is the Hebrew word for "head," and thus some translate it as poppy-head. Support for this claim is that the Latin word caputa means poppy-heads.[14]

The poppy's original home was in Asia Minor, and it went from there to Greece, where it was popular in mythology. According to myth, Ceres created the poppy so she could sleep and forget the loss of her daughter who had been carried off by Pluto.[16] The Greeks must have associated the poppy with both death and sleep, as Thantos (death), Nox (goddess of night), and Hypnos (sleep) were all represented with adorned poppies.

There are also many references to soporifics and

This is one of 11 theses, written by fourth year students at the University of Kansas School of Medicine, selected for publication by the Editorial Board from a group judged to be the best by the faculty at the school. Dr. Collom is now serving his internship at Sacred Heart General Hospital, Eugene, Oregon.

* Macht diagrees and Ebeell does not attempt to translate the hieratic character that Joachim called poppy.

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to opium in ancient Greek literature. In Homer's *Odyssey*[12] (990 B.C.), we find a description of the powers of a drug given to Telemachus, Menelaus, and others by Helen of Troy. "Then Helen, daughter of Zeus, turned to new thoughts. Presently she cast a drug into the wine whereof they drank, a drug to lull all pain and anger, and bring forgetfulness of every sorrow. Whoso should drink a draught thereof, when it is mingled in the bowl, on that day he would let no tear fall down his cheeks, not though his mother and his father died, not though men slew his brother or dear son with the sword before his face, and his own eyes beheld it." A drug of such powers would seem compatible with opium. Helen is said to have received her drug from Polydamna, wife of Thon, the King of Egypt, "where earth the grain-giver yields herbs in greatest plenty, many that are healing in the cup, and many baneful."[12]

According to Xenophon (400 B.C.), a Greek historian, Socrates knew of the sedative action of opium as is seen from the following quotation: "It is my opinion, too, said Socrates, that we drink; wine moistens and tempers the spirits and lulls the cares of the mind to rest, as opium does the body."[25]

The first authentic reference to the poppy and some of its therapeutic actions is found in a book by Theophrastus, a Greek botanist of about 300 B.C. He describes three kinds of wild poppies, which he calls the horned, rhoias, and Herakleia poppies, stating that they are distinct plants, though they come under one name, (i.e., poppy). He says that they can be used "in a posset of mead for epileptics" and can be used for purging, both upwards and downwards.[23]

Heraclides (230 B.C.), the founder of the Empiric School, which rejected anatomy and depended entirely on drugs in the practice of medicine, was the first to record opium as an anodyne in painful diseases.[11]

The use of the poppy in medicine spread from Greece to the Roman Empire, and mention of its use by contemporaries in both cultures will now be considered. In the Golden Age, the century from 80 B.C. to 20 A.D. when Latin literature attained maturity, Virgil and Ovid refer to the poppy.

A quote from Virgil's *Georgics* is as follows: "For the field is drained by flax-harvest and wheat-harvest, drained by the slumber-steeped poppy of Lethe, but yet rotation lightens the labour. . . ."[24]

And from Ovid, the following:

"His son was sick and could by no means rest.
She, as she went into his little mound,
Sleep-pouring poppies gathered from the ground.
The whiles she plucked, she tasted it, 'tis said,
And unawares her long, long fasting stayed;
. . . But Ceres fasted, and in milk lukewarm
Gives poppies to the boy, his sleep to charm."[18]

Celsus (25 A.D.) in his *De Medicina* described ways of preparing medicinals containing opium for "headache or ulceration or ophthalmia or toothache or difficulty in breathing or intestinal gripings or inflammation of the womb or pain in the hips or liver or spleen or ribs . . ." or for "genital trouble," from which "a woman collapses speechless. . . ." Two such medicinals which counteract pain in the above complaints by producing sleep are as follows: "Poppy tears, dried mandrake, apples . . . mixed with raisin wine. Small quantity either swallowed or dissolved in water and taken as a draught.

"Or take a good handful of wild poppy-heads when just ripe for collecting the juice and put into a vessel and boil with water sufficient to cover it. When this handful has been well boiled there, after being squeezed out it is thrown away; and with its juice is mixed an equal quantity of raisin wine, and heated until of the consistency of sordes, (what is scraped off the skin by the strigil after exercise). When the mixture has cooled, pills are formed, the size of our beans."[5]

In his *De Compositiones Medicamentorum,* Scribonius Largus, in about 40 A.D., gives a good description of the method by which opium is obtained from the poppy capsule,[14] and Pliny the Elder, at about the same time, discusses "diakodion," opium, and "meconium." Pliny, in his *Natural History,* states that the "diakodion" preparation is "made with 120 heads—of wild poppy, steeped for two days in three sextarii of rain water, after which they are boiled in it. You must then dry the heads; which done, boil them down with honey to one half, at a slow heat." He states also that others have added to the above recipe, but that this is "so much ostentation; for the virtue of this simple and ancient preparation depends solely upon the poppy and the honey."[19]

Then in the following quotations, Pliny tells how to make opium, and the difference between opium and meconium: "The black poppy acts as a soporific, by the juice that exudes from incisions made in the stalk. . . . This is done at the third hour, in a clear, still, day, or, in other words, when the dew has thoroughly dried upon the poppy. . . . This juice is possessed not only of certain soporific qualities, but, if taken in too large quantities, is productive of sleep unto death even: The name given to it is opium."[19]

Then, "when heads and leaves of the poppy are boiled together, the name given to the decoction is 'meconium'; it is much less powerful, however, in its effects than opium."[19]

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of the opium poppy. The following is taken from a translation of his *Greek Herbal*: ". . . ye common virtue of them (poppies) is cooling. Whence ye leaves and ye heads being sodden in water, and fomented on, cause sleep. . . . But ye heads being sodden by themselves in water to ye half, and then sodden again with honey till that ye moisture be thickened, they make a licking medicine, being lenitive for coughs and distillations of ye artery, and coeliacall affections."[8]

Galen (150 A.D.), who was born in Greece and moved to Rome to practice medicine at the age of 30 years, discussed antidotes and a theriac containing opium. According to him an antidote was used to protect against poison, bites of venomous animals, and affections arising from a faulty diet. The so-called mithridatum, and later theriac, was professed to fulfill all three. Mithridatum was composed by Mithridates, and theriac by Nero's head physician, Andromachus, the latter adding to, and subtracting from mithridatum to prepare his substance. Galen states that "If one takes the drug daily, as did our late Emperor Marcus Aurelius Antoninus"—as well as did Mithridates—"he will be secure against deadly poisons. . . . Thus it is said that when Mithridates preferred to die by poison rather than become subject to the Romans, he could not find anything capable of killing him."[10]

Then Galen makes a possible reference to the addictive powers of opium, the first such reference I have found. "And when he (Antoninus) began to get very drowsy at his daily occupations, he took away the poppy-juice." Then "he began to pass the greater part of the night without sleep. Hence he was forced once more to take some of the mixture which contained poppy-juice, as this had now become more or less habitual with him."[10]

The fall of the Roman Empire in 400 A.D. marked the beginning of the Middle Ages, a period referred to as the Dark Ages because of the cultural decay. This era brought a reduction in the size of Western herbals, but much was to be gained from the knowledge previously accumulated by the Arabian Empire.

From Greco-Roman culture, medical knowledge was acquired for Persia through the efforts of Nestorius (400 A.D.). He was a native of Constantinople but was banned from his country because of certain religious views. He eventually settled in southwestern Persia where he founded a medical school that survived until the tenth century. Nestorius and his followers translated the knowledge they acquired into Syriac in the hope of continuing the brilliant Hippocratic tradition. Thus with the Mohammedan conquest of Persia, the Arabs found medical treasures of the Greeks and Romans recorded on old Nestorian parchments.[15] Arabic medicine, therefore, would seem to be of Persian and, indirectly, of Hellenic origin.

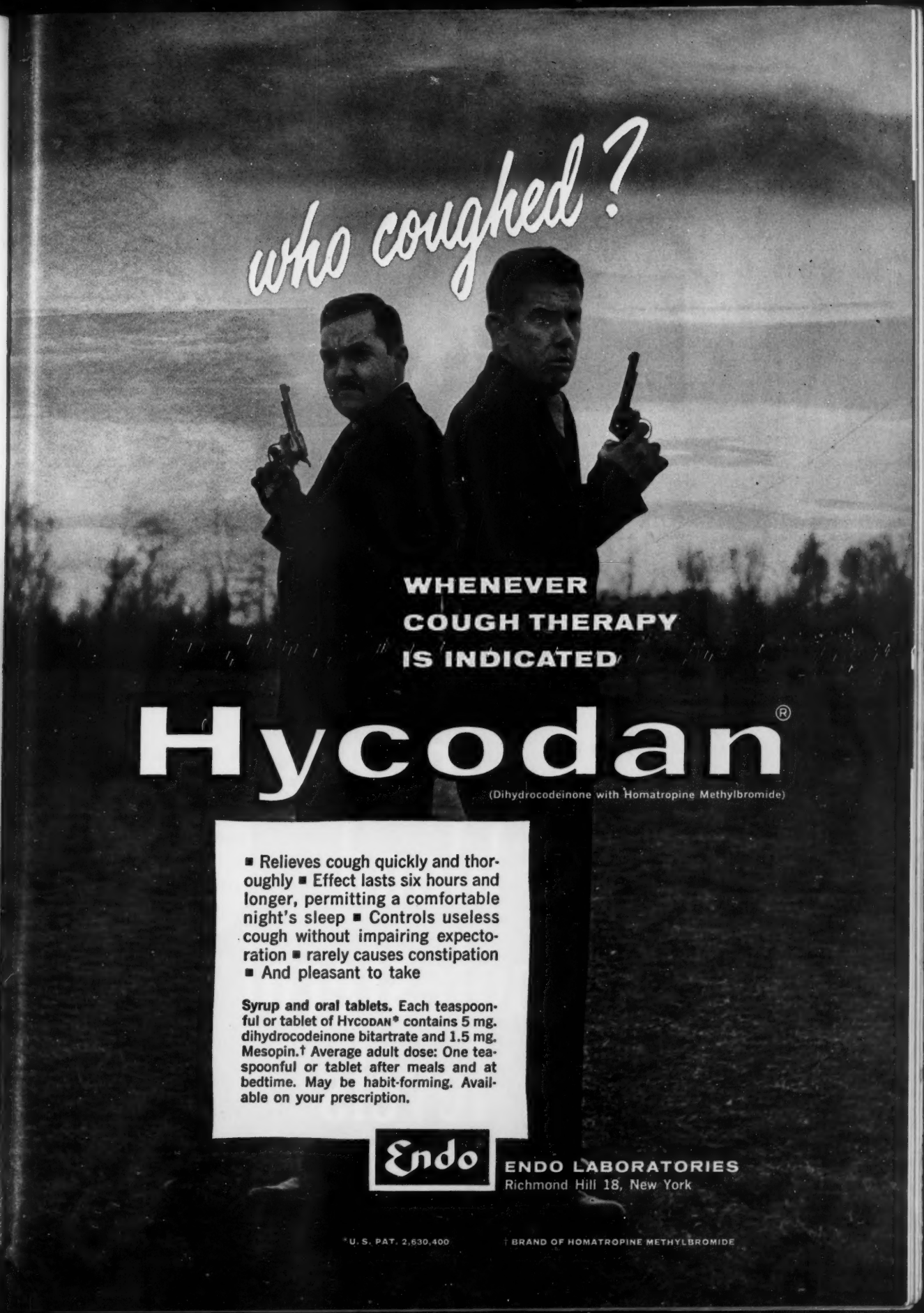
The first reference I could find to the use of opium in the Arabian Empire (eighth to twelfth centuries A.D.) was during the period of Avicenna (about 1000 A.D.) He was the dominant figure of the Arabic School of Medicine, all available medical knowledge of the time being codified in his *Canon of Medicine*. Avicenna states, "The most powerful of the stupefacients is opium. Less powerful are: seeds and root-bark of mandrake; poppy; hemlock; white and black hyoscyamus; deadly nightshade; lettuce-seed; snow and ice-cold water."[2]

Through the Arabs, opium was introduced into India by the spread of Mohammedanism,[14] and into China during the Sung Period (960-1280). Later, Indian traders, then Italian, shipped opium to China. In the early 16th century, Vasco da Gama, by discovering a way around the Cape of Good Hope, opened a new trade route to the Orient for Portuguese merchants. The subsequent influence of opium in India and China will be discussed later in this paper, and now its influence in the West will be followed.

In the late 12th or early 13th century, the leading surgeon of the day was Hugo de Lucca, whose sleeping sponge preparation, used as an inhalation anesthetic, was the basic prescription used by medieval physicians. Hugo was probably educated in Salerno and taught and practiced in Bologna. Unfortunately he left no written records, but his son, Theodoric of Cervia, describes his surgery and the "spongia somnifera" in detail. In the *Surgery of Theodoric,* the great surgical work of the 13th century, we find that the recipe for the "spongia somnifera" contains an ounce of opium along with other present day herbs. The ingredients were mixed in a brazen vessel, and a sponge was placed in it. Then, according to Robinson,[20] Theodoric says to "let the whole boil, as long as the sun lasts on the dog-days, until the sponge consumes it all, and it is boiled away in it."

In the middle 14th century, John Arderne, an Englishman and the originator of the operation for fistula in ano, used salves and elixirs containing opium in the following ways: "Anoynt his front, his pulses, his temples, his armeholes, and his lones of his heud and his fete, and alsone he schal slepe so that he schal fele no kuttyng. . . . Also one grayne of opii thebaici to the quantite of drams ss, distempered with a pynte of wyne or more after the mist of hym that schal drynk it, schall make hym that drynketh it for to slepe."

Arderne cautioned those who used medications containing opium against inducing too profound a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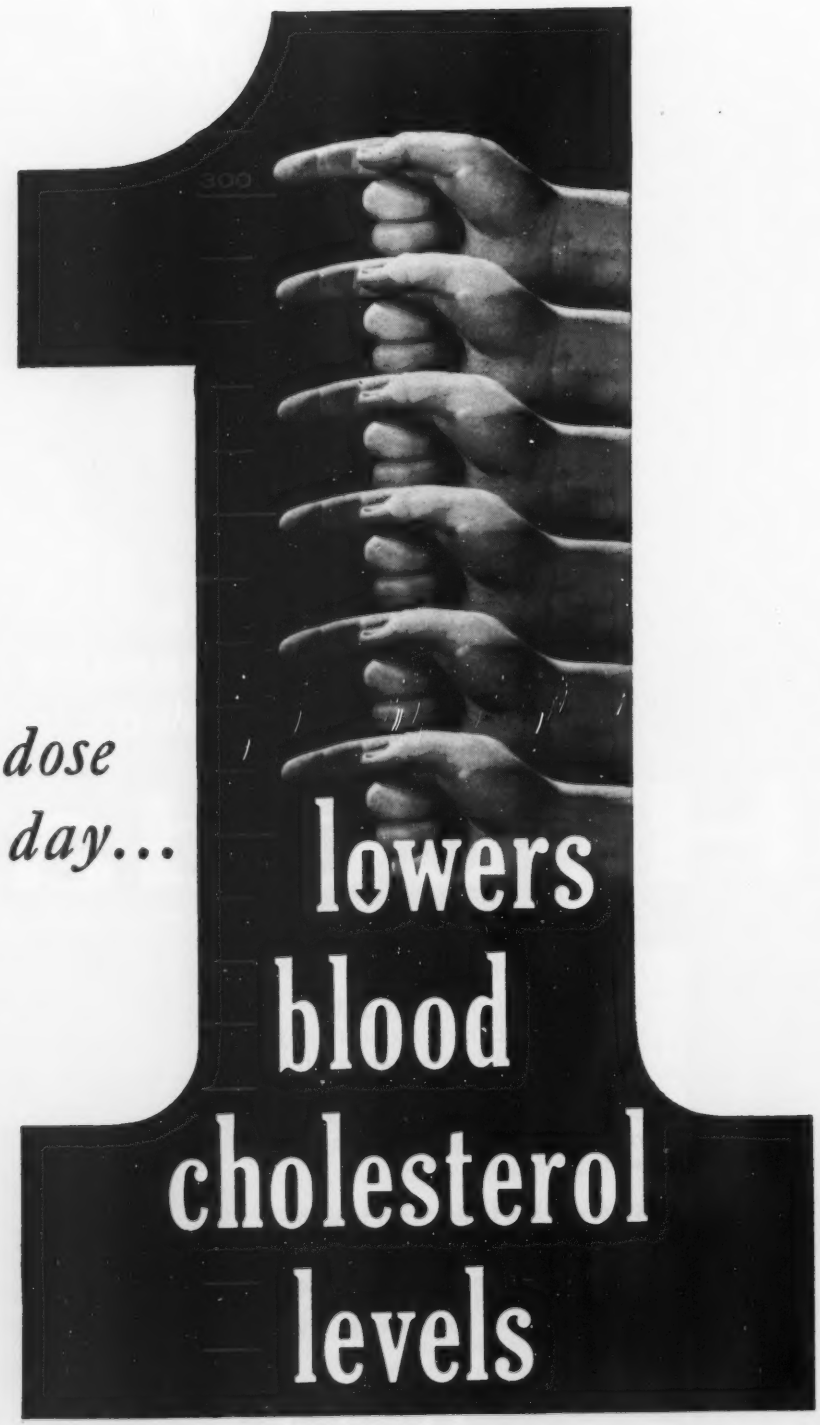

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sleep and offered the following method of arousing the patient: ". . . And witte thou that it spedeth for to draw hym that slepeth so by the nose and by the chekes and by the berde, that the spirites be quickened that he slepe nost ouer ristfully."[1]

Towards the close of the Middle Ages, and with the beginning of the Renaissance, we find mention of narcotics in general literature. Boccaccio, who survived the Black Death in 1348, and Chaucer describe the use of opium. In the *Decameron* of Boccaccio[3] is found a story about a famed physician of Salerno, Master Mazzeo, who was called upon to amputate a gangrenous leg. He was of the opinion that the pain of such an operation could be endured only by the use of an opiate. The physician distilled "a certain water of his composition, which, being drunken by the sick man, should make him sleep so long as he deemed necessary for the performing of the operation. . . ." The potency of the compound was later brought out when the lover of the physician's wife drank the water by mistake, and the wife, supposing the man's deep sleep to be death, put him into a chest.

In Chaucer's *Canterbury Tales* is found the following passage:

"That soone after the mydnyght, Palamon,
By helpyng of a freend, brak his prison,
And fleeth the citee faste as he may go.
For he hade yeve his gayler drynke so
Of a clarree maad of a certeyn wyn,
Of nercotikes, and opie of Thebes fyn,
That al that nyght thogh that men wolde hym shake,
The gayler sleep, he myghte nat awake."[6]

Then in a much later period we find reference to the poppy in the literature of Shakespeare in the following passage from *Othello*:

"Not poppy, nor mandragora,
Nor all the drowsy syrups of the world,
Shall ever medicine thee to that sweet sleep
Which thou ow'dst yesterday."[21]

In the early 16th century came the famous Paracelsus (a name meaning greater than Celsus), who first used the term "laudanum" for a secret preparation of his own making. Paracelsus is interesting in that he possessed no medical degree, although he acquired considerable real knowledge of medicine and lectured on medicine at the University in Basel, Germany, in 1526. His lectures were preceded by a solemn burning of the works of Galen and Avicenna, and the lectures themselves discredited past and contemporary medicine, setting forth his own theories and methods of treating disease. Though it is not known if his "laudanum" contained opium, for more than a century after Paracelsus, the term laudanum was applied to solid preparations, some of which did contain opium.[13]

The alcoholic tincture which we now know as laudanum was originated by Thomas Sydenham in 1669. Sydenham, the father of English medicine, is known better by name than by his writing, and his writings are better known than the events of his life. But one thing of Sydenham is certain, and that is his praise for opium which follows: "And here I cannot but break out in praise of the great God, the Giver of all good things, who hath granted to the human race, as a comfort in their afflictions, no medicine of the value of opium, either in regard to the number of diseases that it can control, or its efficiency in extirpating them. . . . Medicine would be a cripple without it; and whoever understands it well, will do more with it alone than he could well hope to do from any single medicine."[22]

Thomas Dover, once a student of Sydenham, is another interesting character in medical history. Osler[17] says, "Thomas Dover, the Doctor, has drifted into our modern life on a powder label (to which way of entering the company of posterity, though sanctified by Mithridates, many would prefer oblivion) even to continuous immortality on a powder so potent and palatable" as that of Dover's opiate compound.

Dover is also remembered as a buccaneer who promoted and took part in a privateering expedition to the South Seas in 1708, an expedition which resulted in the rescue of Alexander Selkirk (Defoe's Robinson Crusoe) from Juan Fernandez Island in February 1710, and resulted in the realization of booty valued at 170,000 pounds sterling. Upon his return to England, Dover set himself up in the practice of medicine, though the "spirit of the buccaneer was not dead in the old man, as no occasion is missed either to blow his own trumpet, or to tilt a lance at his colleagues."[17]

Dover left to medicine his *Ancient Physician's Legacy to His Country* from which the following is taken: "It has been objected to one part of my book, that I have a great dislike to opiats; and yet, that in the prescription immediately following, I have set down an opiat. Some apothecaries have desired their patients to make their wills, and settle their affairs, before they venture upon so large a dose as I have recommended, which is from 40 to 70 grains. As monstrous as they may represent this, I can produce undeniable proofs, where a patient of mine has taken no less a quantity than an hundred grains, and yet has appear'd abroad the next day."[9] He explains further that the other ingredients that are mixed with the opium diminish its potency.

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containing opium sprouted out in the 17th and 18th centuries such as Matthew's Pills, Starkey's Pills, Black Drop, and paregoric. Both paregoric and laudanum (mentioned earlier) were titles given to a variety of preparations listed in the *Pharmacopoeias,* the common ingredient of all being opium.[13]

Of great historical interest is the spread of the opium influence in China and India during the last half of the 18th century. Through Portuguese merchants and, later, through the Dutch East India Company, Chinese importation of opium increased rapidly. Opium smoking came in during the era of Dutch control and, indirectly, was an American contribution. After Sir Walter Raleigh introduced tobacco into England from America, the Dutch thought of smoking opium and contrived a blend of tobacco and opium. By the resultant increase in opium trade to both India and China, the history of the world was altered.

Opium trade and production was in large part responsible for the war between England and France for control of India, for the English conquest of India for control of the latter's opium production, for England's two wars with China in 1839 and 1851 which have been called the Opium Wars, and for the moral degeneracy of millions of Orientals.

Also of historical interest is the great Persian famine of 1871-1872 which resulted from most of the arable land in Persia being sown with poppy seeds.

I will not end a story of opium on a note of degradation or human suffering, but choose rather to conclude by telling a story of the discovery of the active principle of opium, the alkaloid responsible for the pain-relieving quality of this ancient herb.

In 1803 a drug clerk, while working in an apothecary shop at Paderborn in Prussia, looked at a piece of crude opium gum and was curious about the ingredients it might contain. His curiosity led him to extract a piece of the gum in water, and then to add ammonia to the extract, therby obtaining some crystals. He went no further with the simple experiment at this time. Then several years later, after he had established a pharmacy of his own, he invited three friends into his shop. He related to the friends how he had obtained crystals from gum opium, and that he had found that the crystals put dogs to sleep. The difficulty at this time, he added, was that the proper amount of the crystals to be given to man for similar results was undetermined. The purpose of the invitation was beginning to clarify itself to the guests. They expressed their willingness to sacrifice for science, but pleaded that it be a little dose at first. The host replied that only half a grain washed down with alcohol and water would be used.

During the subsequent "human" experiment, the host put down a description of his own sensations. After the first one-half grain dose he noted that his face began to flush. With the second dose, 30 minutes later, he became somewhat nauseated and then lethargic and numb. Then following the third dose, after another 30-minute period, he became dreamy with marked depression, concluding that the point of poisoning had been reached. The conclusion was right.[7]

The man of this classical experiment and description was Frederick Wilhelm Serturner, the discoverer of morphine. The Greek god of dreams, Morpheus, had indeed been honored.

In all, this has been the story of an ancient herb, the "tears" of the poppy, which, as no other herb, has been referred to in great historical and literary works, has influenced the course of history, causing famine and war, and has influenced the lives of millions of people, causing much grief and yet giving much relief. This has been a paradoxical herb, unsurpassed for causing misery through its addictive powers, but unsurpassed also as a reliever of pain and anxiety perhaps never to be replaced by modern "new" drugs.

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1. Locket, S.: Brit. M.J. *1*:809 (Apr. 2) 1955.

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Nutrition in Pregnancy

Because nutrition plays such an important role in all phases of reproduction, the A.M.A.'s Council on Foods and Nutrition has selected "Nutrition in Pregnancy" as the title of its 1957 symposium. The meeting will be held October 11 at the University of Missouri Medical Center, Columbia, Missouri. Joint sponsors with the A.M.A. are the University of Missouri Medical School and Adult Education and Extension Service and the Boone County Medical Society.

The symposium will provide an excellent opportunity for physicians, nutritionists, dietitians, nurses, and others to acquaint themselves with current findings in nutrition and the practical application of these findings to the management of obstetrical patients.

Topics to be discussed include: the influence of maternal nutritional level on the fetus and infant; metabolic and biochemical changes in normal pregnancy; importance of nutritional state of mother prior to conception; nutrition experiments as an instrument of teratologic research; the effect of the reproductive cycle on nutritional status and requirements; dietary habits during pregnancy; panel discussion to review epidemiologic studies.

In the past 56 years mortality from tuberculosis has declined from 199 to 8 per 100,000 population, according to Health Information Foundation. While this is remarkable progress, the Foundation notes, tuberculosis is still a great health problem, with 100,000 new cases reported in the United States in 1955.

Sodium and Potassium

(Continued from Page 584)

never exceeds normal values, and the retention of sodium is not as pronounced as in patients who are not given such therapy. From the foregoing there would seem to be a definite therapeutic indication for administering potassium by mouth. On the other hand, it would seem that sodium is not only useless but might even be contraindicated during this period.

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More than 100,000 disabled workers during August received checks under the Old Age and Survivor's Insurance disability payment program, the first group to receive the benefits. The program went into effect in July, and the August payments are for that month. Disabled workers whose applications are filed before the end of the year will be paid retroactively for all months from July on, but starting in 1958, O.A.S.I. will not make payments for any month prior to filing of the application.

Work is going forward on the formation of state and county chapters of the Medical Service Society of America, a national organization of professional ethical medical detail men. Mr. Noble S. Birkett, Oklahoma City, is president of the association.

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BOOK REVIEWS

Goepp's Medical State Board Questions and Answers. Ninth Edition. By Harrison F. Flippin, M.D. Published by W. B. Saunders Company, Philadelphia. 659 pages. Price $8.00.

This book should be of particular interest to any doctor who plans to take a state board examination for licensure. In addition, this book is a valuable source for review for any doctor who is interested in a wide coverage of the medical field in the form of questions and answers. The chapter on medical jurisprudence should prove the book's worth to any doctor.

The editor and editorial board who made this publication possible have fulfilled the aims of the original author, namely to present to the student of medicine reliable, up-to-date medical information in convenient, concise, and adequate form.—*O.W.D.*

An Atlas of Cardiac Surgery. By Jorge A. Rodriguez, M.D. Published by W. B. Saunders Company, Philadelphia. 250 pages. Price $18.

The book is attractively bound and although of nonstandard size is convenient to handle. It lies flat when opened, and the arrangements of the text and illustrations are clear and inviting. The book was prepared by the artist and author after visiting clinics of the outstanding American surgeons interested in surgical treatment of the diseases of the heart. The book is divided into six sections and index. The sections are as follows:

1. Surgical Anatomy of the Heart and Great Vessels.
2. Adjuvants Cardiac Surgery, including instruments and adjuvant devices, special considerations in anesthesia, hypothermia, and mechanical extracorporeal circulation.
3. Surgery of the Great Vessels, including patent ductus arteriosus, coarctation of the aorta, aneurysms of the thoracic aorta, vascular rings, aorticopulmonary fistula, and transposition of the great vessels.
4. Surgery of the Valves of the Heart, including mitral stenosis, mitral insufficiency, pulmonary stenosis, and aortic insufficiency.
5. Surgery of Congenital Defects of the Heart, including tetralogy of Fallot, atrial septal defects, and ventricular septal defects.
6. Pericardiectomy, Revascularization Procedures, Wounds of the Heart, and Cardiac Arrest.

The information in each section is authentic and is ably illustrated. The section on surgical anatomy of the heart and great vessels is written from the standpoint of the surgeon and although the detailed anatomy that would be preferred by the pure anatomist is not described, there is adequate detail for an understanding of surgical procedures. The information recorded in the section under adjuvants to cardiac surgery is written in summary form and is well done. Significant details are given, and the overall estimate of the significant factors is complete.

Descriptions of the various techniques of surgery are those carried out by recognized authorities. The illustrations are clear and are easily followed. The complications encountered during various procedures are also considered, and methods of management given adequate emphasis.

There is a minimum number of factual, typographical, and illustrative errors. The book is well indexed, and desired information can be quickly procured. I would consider it an outstanding surgical atlas and worthy of a place in the library of all persons interested in diseases of the heart.—*F.F.A.*

Physical Diagnosis—Correlation of Physical Signs with Certain Physiological and Pathological Changes in Disease. Second Edition. By Simon S. Leopold, M.D. Published by W. B. Saunders Company, Philadelphia. 537 pages, 379 illustrations, 25 color plates. Price $9.00.

The first edition of this excellent text was published in 1932, the author being assisted by several of his Philadelphia colleagues who contributed chapters concerning their own special interests. These same authorities have collaborated in the revision and writing of the second edition.

The author has succeeded in correlating physical findings and clinical picture with the basic pathology, etiology, and disturbed physiology responsible for particular findings. Particular emphasis is given to methods of taking a satisfactory history, 34 pages being used for this purpose. Experienced physicians will find this section of the volume helpful, especially the portion devoted to the psychiatric survey.

All the chapters are well written and excellent for teaching of medical students. The contributors have helped to make several of the chapters especially valuable and worth study by all physicians. The chapter on Sounds from the Thorax: Acoustic Principles by S. Reid Warren, Jr., is helpful in making one understand and interpret physical findings properly, in addition to imparting proper methods to elicit such findings. The chapter on the circulatory system is thorough; the illustrations, especially the phonocardigrams, help the examiner understand better

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the time relationships between the waves in the electrocardiogram, heart sounds, and the types of murmurs observed with various valvular functional abnormalities.

The chapter on the neurological examination is thorough, easy to read and comprehend. The chapter on pediatric examination is especially helpful to the student, general practitioner, and pediatrician alike.

This edition contains a thorough presentation of the methods of physical examination and interpretation of the findings for each of the systems. This volume would be useful in any physician's library.—*C.C.U.*

The Pharmacology of Psychotomimetic and Psychotherapeutic Drugs. Annals of the New York Academy of Sciences. Edited by Otto V. Whitelock and Frank N. Furness. Published by the Academy, 2 East 63rd Street, New York 21, New York. Price $5.00.

This is an important work in the present era of increasing interest in study and use of drugs that influence man's mood and behavior. Since the work contains much material of a highly technical nature, this review will limit itself to those items of particular interest to the clinician.

Part I (Clinical and Biochemical Aspects of the Psychotomimetic Agents) opens with Osmond's review of the clinical effects of psychotomimetic agents. Our Canadian colleague, well known for his work in this field, writes clearly and lucidly to highlight this section of the work. His own choice of a term for these drugs is "psychedelic," meaning "mind-manifesting."

In his article "Neurochemistry and Serotonin: A Chemical Fugue," Dr. Irving H. Page describes how an interest in a problem of cardiovascular disease 28 years ago played its part in the research that led to the discovery of serotonin.

Parts IV and V will probably be of greater interest to the practitioner. Part IV deals with the clinical, behavioral, and pharmacological effects of psychotherapeutic drugs, while Part V deals with neurophysiological and biochemical effects. Outstanding is the survey by Margolis entitled "Pharmacotherapy in Psychiatry: A Review," the result of a survey to determine the value of chlorpromazine and reserpine. In the diversity of opinions expressed about the usefulness of these drugs and the techniques in their utilization, every physician will find opinions with which he may agree or disagree.

Despite many studies, including those published in this volume, there is not yet at hand convincing neurophysiological evidence to explain the site and mode of action of ataractic drugs (reserpine, chlorpromazine, and others). The fact that we have only minimal understanding of the chemistry and physics of normal thought is a basic lack. Add to this lack of knowledge the fact that the problems of human psychopharmacology are many and difficult, and one can easily see how complex is the task of determining the biochemical mechanisms by which these drugs act. The work of the thoughtful and dedicated researchers reflected in this volume is highly commended.—*I.K.*

The Doctor as a Witness. By John Evarts Tracy. Published by W. B. Saunders Company, Philadelphia. 221 pages. Price $4.25.

With the universal increase in the liability claim, more and more physicians are being invited to offer medical opinion and display their medical knowledge in courts of law. These are strange environs to the average physician for the display of his special knowledge, training, and experience, and often the rules of behavior are quite foreign to this same training and background.

It is, therefore, refreshing and most useful to have available in such clear and readable fashion the material organized in *The Doctor as a Witness.* Not only are the rules of behavior carefully explained and the reasons behind them delineated, but special suggestions to the physician to assist him in participating in such events are lucidly presented. Individual chapters are devoted to the special circumstances of Workmen's Compensation proceedings and of malpractice cases, and particularly important is the chapter devoted to instruction as to what makes a good medical witness. This small but most useful and readable book should be available to every physician and particularly those who frequent the arena of medical legal practice.—*J.A.S.*

Practical Gynecology. Second Edition. By Walter J. Reich and Mitchell J. Nechtow. Published by J. B. Lippincott Company, Philadelphia. 647 pages. Price $12.50.

This volume justifies its name in that it is written with major emphasis on the therapy and management of gynecologic disorders. The style is informal: it seems to be a compilation of lecture material and has an easy-to-read conversational quality as distinguished from some of the more formal and stilted texts. Its at-times-breathless pace and frequent admonitions to think of this and not forget that, however, remind one of the lecturer whose emphasis on his specialty brings moans from the student body because he seems to feel that his subject should always take priority

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in the student's mind. Which reminds us, in turn, of our medical school roommate who always contended he would have to specialize because he was not smart enough to be a general practitioner.

It is a better text for the student than he is apt to realize for he tends to think of gynecology only in terms of prospective surgery, not realizing how much office work will fall in this category. This book wisely avoids overextension into surgical techniques and thereby establishes itself as a helpful reference for diagnosis and a practical guide to office treatment. It is liberally and excellently illustrated. In particular, the color plates are clear and faithful in color values. —*D.E.G.*

The Chemistry and Biology of the Purines, Ciba Foundation Symposium, G. E. W. Wolstenholme and C. M. O'Connor, Editors. Published by Little, Brown and Company, Boston. 327 pages. Price $9.00.

A wide variety of aspects of the class of purines is treated in this book. From fundamental physicochemical properties of purines to the clinical uses thereof, the subject matter is well presented by recognized authorities in the field. Almost no discussion is devoted to the historical development of purine research, and practically all the discussion concerns the results of recent research.

It is not likely that all readers will find every presentation in the symposium of interest because of the scope of the symposium. Although the material is well given and documented in general, the discussion after each presentation is occasionally vague and incompletely and inconsistently documented.

On the basis of their development, clarity and import, the best sections seem to be the following: "The Use of 6-Mercaptopurine in the Treatment of Leukemia" by D. A. G. Galton, "Puromycin" by B. L. Hutchings, "On the Activation of the One Carbon Unit for the Biosynthesis of Purine Nucleotides" by G. R. Greenberg and L. Jaenicke, and "The Enzymatic Synthesis of Inosinic Acid *de novo*" by J. M. Buchanan et al. Although the symposium was held more than a year ago, the most significant material presented is still the latest word in purine research.—*L.C.M.*

The Fight for Fluoridation. By Donald R. McNeil. Published by Oxford University Press, Inc., New York. 241 pages. Price $5.00.

This is a well-written and factual description of the development of fluoridation, a proved public health measure which materially reduces the rate of dental decay, the most common chronic disease of mankind and the most prevalent of all childhood afflictions.

Dr. McNeil has described very interestingly the history of fluoridation, beginning with Dr. Frederick S. McKay's early investigation, in 1901, of the "Colorado brown stain."

The author reports on the completion of the two leading ten-year research studies, begun in 1945 at Grand Rapids, Michigan, and Newburgh, New York, demonstrating that fluoride added to a fluoride-deficient public water supply reduces the rate of dental decay by approximately 60 per cent. He pointed out that the findings should aid the proponents in answering the opponents' earlier plea to "wait until the experiments are finished."

The author gives an account of the public controversies which have arisen in some areas where fluoridation was being considered, specifically pointing to the early heated conflicts experienced in Wisconsin with the opponents of fluoridation. He also relates some of the tactics employed by the opponents of fluoridation.

The Fight for Fluoridation is recommended reading for anyone interested in the fluoridation of public water supplies.—*W.R.B.*

A Woman Doctor Looks at Love and Life. By Marion Hilliard. Published by Doubleday and Company, New York. 190 pages. Price $2.95.

Dr. Hilliard says, "I have been watching the many lives of women for a quarter century; the adolescent with her terrible fears, the young wife with her dismay at love-making, the unmarried mother with terror in her eyes, the career woman with her longings, the older woman with her loneliness. I know them all and I would be insensitive and a poor doctor if I didn't try to help."

In this book she certainly has done just that. It is a series of informal discussions on the many problems of women of all ages. Dr. Hilliard is sometimes outspoken, but always realistic. To all women she advises, "Don't waste your strength in being outraged because life is difficult for you. Assume that life naturally is difficult, will never be easier. Accept the inevitables and live vigorously."

To the expectant mother, "The drama of birth, the torment wrapped with exultation beyond self, is the truest and finest moment a woman can know."

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On old age: "Retirement, I feel, means a new adventure in living—not a stopping."

Excerpts from this book have already been published in *Reader's Digest* and *Pageant* and perhaps others.

This reviewer is ordering copies of the book to lend to patients. He believes it could almost be called a "Handbook for Living" for women.—*N.H.O.*

The Changing Patient-Doctor Relationship. By Martin G. Vorhaus, M.D. Published by Horizon Press, New York City. 310 pages. Price $3.95.

If you wish to improve in the "Art of the Practice of Medicine," this is your book! Application of the new psycho-social approach to the patient-doctor relationship will result in better doctors and happier patients.

Too infrequently the patient leaves the doctor's office with the feeling that the doctor is a wonderful person. "He knows his stuff. He gave me a fine examination and really put his finger on my problem. I'm sure he's going to help me."

Too seldom does the doctor usher out the patient with the feeling, "There goes a sensible cooperative patient. He'll follow my recommendations and reap benefit. What a pleasure it is to take care of a man like that! Why aren't there more like him?"

This book is a study in a means to an end: to bring the doctor and patient into the closest rapport, so the doctor may fulfill his obligations to the patient.

After an academic description of the patient and how he became one, and of the doctor and how he became one, the author portrays the doctor as a builder of bridges and shows how the bridges of learning, accepting responsibility, resolving conflicts, acquiring empathy, integrating the patient's attitudes with his illness, striving for personal balance in subjective reactions, and maintaining flexibility in personal adjustments, can make a good doctor of a scientifically trained healer.

An unusual feature of this book is the presentation of five long and detailed case histories which illustrate how the changing patient-doctor relationship has benefitted all those concerned.

Because anxiety is man's number one malady at present, the need for psychotherapeutic guidance is increasing. This is a service the doctor must offer along with pills, shots, and operations. Because the patient and his environment are always changing, so must the doctor be changing. He must change from a novice to a master, but more than this he must forever be as changing as the patient, as a person. He must always modify his values and broaden his horizons. As he better understands his patients, so does he better understand his friends and his family. He has better insight about others—and above all about himself! The doctor learns that he is not a creator, but the servant of the Creator. Only the patient can and should make of his life what he desires. To know what is best for the patient is not the point or end of the problem or case. The patient must find it out, accept it, and completely put it into action before the doctor can achieve success with his patient.

Reading this book will make you a better doctor! —*C.M.B.*

Therapeutic Exercise for Body Alignment and Function. By Marian Williams, Ph. D., and Catherine Worthington, Ph. D. Published by W. B. Saunders Company, Philadelphia. 127 pages. Price $3.50.

This manual is a revised and somewhat enlarged version of a syllabus published several years ago by the same authors. Both are physical therapists with a background of physical therapy education, and they state that the manual is designed for the use of all persons dealing with problems of body alignment and function. However, reference is made in the text only to physical therapists; the word physician never appears, nor is there any evidence of interest on the part of the authors to suggest that therapeutic exercises are an important part of medical treatment and that close liaison with the physician is necessary.

The manual is divided into several convenient areas: a definition of normal posture, methods of testing for and recording of body alignment, a section concerned with general features of the therapeutic exercise program, the principles of exercise treatment specifically applied to various body areas, positions of the body in activity and rest and, finally an appendix which reviews the anatomical location and role of the primary muscles concerned with body alignment and function. The text is brief, is written in a clear, concise style, and is profusely illustrated

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with sketches which demonstrate the pertinent details of the text in superb fashion. It is difficult to conceive a text that would teach therapeutic exercise, within the above limits, more admirably.

It is disappointing to find no reference to the physiology of therapeutic exercise. Reference is made to electromyographic studies, to general reflex activity, and to muscle tone, but cognizance is not taken of the important physiological studies of muscle, circulatory and nervous system as related to therapeutic exercise. The concept of therapeutic exercise as resting solely on rigid considerations of structural anatomy is steadily giving way to the more complex but more realistic one of changes in the dynamic functional balance of movement patterns in rest and in motion. In this latter area lies a greater field than contemplated in this manual.

Physical therapists and nurses, especially in their student and early graduate days, will find the manual a valuable one. Physical education majors will gain the same benefits. Physicians and medical students would do well to acquaint themselves with this manual to supplement the scanty training in therapeutic exercise given in modern medical curriculums. —*D.L.R.*

ANNOUNCEMENTS

The University of Nebraska College of Medicine announces a series of courses for the 1957-1958 year: September 30-October 2, electrocardiography I; January 16-17, obstetrics and gynecology; February 7-8, endocrinology; March 12, diseases of the skin; April 7-8, pediatrics; April 9-11, postgraduate assembly and Poynter lecture; May 7, trauma; May 8-9, allergy. Courses approved for credit by A.A.G.P. Information from Office of Postgraduate Affairs, College of Medicine, Omaha, Nebraska.

Course in orthopedic surgery and fractures, University of Texas Postgraduate School of Medicine, El Paso, September 29; followed by scientific meeting of American Fracture Association, Hotel Cortez, El Paso, September 30-October 2. Both approved for credit by A.A.G.P. Address El Paso County Medical Society, 1301 Montana Street, El Paso.

Convention of American College of Gastroenterology, Somerset, Boston, October 21-23, followed by course in postgraduate gastroenterology, October 24-26, with Dr. Owen H. Wangensteen and Dr. I. Snapper as moderators. Advance registrations, American College of Gastroenterology, 33 West 60th Street, New York 23, New York.

Course in occupational skin problems, Departments of Preventive Medicine and Dermatology, University of Cincinnati, and U. S. Public Health Service, at Kettering Laboratory, Cincinnati, October 28-November 1. Limited registration. Write Institute of Industrial Health, Kettering Laboratory, Eden and Bethesda, Cincinnati 19, Ohio.

Symposium on fluorides, December 9-11, Institute of Industrial Health, Kettering Laboratory, Eden and Bethesda, Cincinnati 19, Ohio.

Two-week course in radiological safety, January 6-17, Institute of Industrial Medicine of New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York. Tuition $90.

Sectional meetings, American College of Surgeons: Dallas, January 9-11; Jackson, Mississippi, January 16-18; New York City, March 3-6; Salt Lake City, March 17-19; Des Moines, March 27-29. Annual clinical congress, Chicago, October 6-10, 1958.

Twenty-fifth annual session, Omaha Mid-West Clinical Society, Sheraton-Fontenelle Hotel, Omaha, November 4-7. List of speakers on Page 645, this issue.

The Bureau of Public Assistance reports that incomplete statistics indicate that hospital care is the most expensive item involved in the medical care of individuals supported by federal-state public assistance programs. Involved are four categories: the needy aged, blind, dependent children, and permanently and totally disabled. In addition to helping states pay for these people's support, the U. S. also sets aside additional money for their medical bills, money which must be matched in part by the states. The bureau's survey, for July-December, 1956, includes data from 20 states. Hospital care accounted for 37.9 per cent of the medical costs, nursing homes and home care maintenance for 29.5 per cent, drugs and supplies for 13.8 per cent, physicians' services for 13 per cent and other services for 7.9 per cent. The bureau now is attempting to obtain more complete information from a larger number of states on the cost breakdown in the various items of medical care under public assistance.

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THE MONTH IN WASHINGTON

Editor's Note. The following summary of Washington news was prepared by the Washington office of the A.M.A. for distribution to state and regional medical journals.

If dangerous epidemics of Asian flu break out in the country this fall and winter, the medical profession will have its hands full. But the doctors won't be taken by surprise, nor will they lack specific information on proper treatment.

While the attacks in the U. S. were still sporadic and the death rate low—three fatalities in the first 11,000 reported cases— a number of major, nationwide efforts were under way to combat the disease in the months when influenza rates generally are the highest.

1. Acting in coordination with U. S. Public Health Service, the American Medical Association was pressing forward with its campaign to insure that all physicians are informed of how to deal with the disease.

2. In line with recommendations of the A.M.A. committee, a number of state medical societies by mid-August had laid out complete emergency plans, ready to be put in operation if needed.

3. U. S. Public Health Service epidemic intelligence experts were scanning the country for outbreaks that might be Asian influenza, and others were investigating acute respiratory diseases. P.H.S. also set up machinery to keep the medical and health professions informed on nationwide developments in the influenza picture.

4. Advising Surgeon General Burney was a special committee, which included representatives from A.M.A., American Academy of Pediatrics, American Academy of General Practitioners, and the Association of State and Territorial Health Officers.

5. Manufacturers of the vaccine, by running their plants on two or three shifts and seven days a week, were hoping to have produced 60,000,000 cc. by February 1.

There was, of course, the possibility that with Congress in session through most of the summer a vast federal program would be set up, with the U. S. purchasing and allocating the vaccine. It was heartening to the medical profession that this possibility was pretty well eliminated in the early stages when the Department of Health, Education, and Welfare announced the following as official policy:

"The Public Health Service, in cooperation with the medical profession, will stimulate and promote a nationwide voluntary program of vaccination against the prevalent strain of influenza. It will not, however request federal funds for the purchase or administration of vaccine—except for its own legal beneficiaries. The State and Territorial health officers and the American Medical Association have jointly assured the Surgeon General that community resources, both public and private, will be mobilized to provide vaccinations for persons who are unable to pay for such protection."

This policy was reaffirmed later by the White House, when the President asked for half a million dollars to finance the additional work for Public Health Service. The White House statement said flatly that it did not plan to have the federal government buy vaccine.

The A.M.A.'s Board of Trustees selected as members of the special committee the same physicians who make up the Civil Defense Committee, with Dr. Harold C. Lueth as chairman. In addition to the work of this committee, special articles are being published in the *A.M.A. Journal,* mass circulation media are being used to bring information on Asian influenza to the lay public, and the A.M.A. Council on Drugs is investigating and reporting to physicians on the use of antibiotics in treatment of the disease.

Notes

To wind up a long investigation of the safety of chemical additives to foods, a House committee called in a panel of scientists for two days of discussion. In general they concluded: Be careful about any mandatory federal controls.

Another hearing on weight-reducing preparations sold over-the-counter in drugs stores heard a parade of witnesses, all of whom had about the same opinion: In themselves, the pills all are virtually useless in inducing loss of weight, but their other effects range from harmless to definitely dangerous.

Veterans Administration is increasing fees to physicians under the home-town care program, with the new schedules varying by states and areas. During this fiscal year VA will pay out $8 million under this program.

A former A.M.A. president, Dr. Elmer Hess, now heads two government advisory committees, the Health Resources Advisory Committee to Office of Defense Mobilization and the Medical Advisory Committee to Selective Service, membership of which is the same. He succeeds Dr. Howard Rusk.

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THE KANSAS PRESS LOOKS AT MEDICINE

Editor's Note. In this section the JOURNAL *reproduces editorials relating to medicine which have appeared in the lay press. An effort is made to include both favorable and unfavorable comments, and the Editorial Board in no instance assumes responsibility for the opinions expressed.*

Socialized Medicine

"We have had amply demonstrated to us that medicine and politics do not mix." Such reports a magazine that should speak with authority—the *British Medical Journal*.

Britain has had socialized medicine for many years and her National Health Service employs something like 99 per cent of all British doctors.

The service's current troubles have been in the news considerably lately with the most publicized issue being doctors' pay. Such pay is reportedly extremely low by any reasonable standard.

There does, however, appear to be even more to the matter than the economic issue.

As the medical journal puts it, "The employes have lost all trust and confidence in their monopoly employer." As evidence, it points to the fact that in recent months there has been a striking increase in the number of doctors investigating the possibility of leaving England for one of the Dominions.

What are the troubles, other than the salary problem, that socialized medicine has brought to Britain's doctors: The *Journal* has this to say: "The pettifogging arguments about whether a food is a drug, the form-filling, the regulations, earnest discussions on whether a week's leave not taken one year can be carried on to the next, ever-increasing intrusion of the administrator centrally and locally—all this and much more is turning medicine into an administrator's maze. . . ."

The *Journal* then makes the most ominous statement of all, "The unfortunate doctor soon loses his sense of direction and will end up by losing his sense of profession."

Measures are periodically proposed in this country which would give the government sweeping and varied controls over doctors and medical practice, and thus set the stage for ultimate socialized medicine.

We can profit by England's costly mistakes—and thus avoid such schemes like the plague.—*Pratt Tribune, June 17, 1957.*

The death rate from pneumonia, influenza, and tuberculosis has dropped about 90 per cent since 1900 in the United States, Health Information Foundation reports. The improvement is attributed to medical advances, particularly new drugs, and to better living conditions.

More than 52,000 Americans were injured in carbicycle mishaps in 1956.

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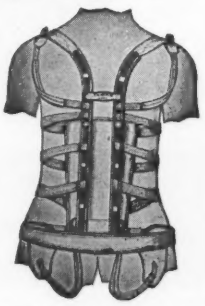

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Carleton B. Chapman, M.D., (Internal Medicine) Professor of Medicine, University of Texas Southwestern Medical School, Dallas, Texas.

Frank C. Coleman, M.D., (Pathology) Assistant Clinical Professor, Department of Pathology, University of Nebraska College of Medicine, Omaha, Nebraska.

Edmond L. Cooper, M.D., (Ophthalmology) Instructor in Ophthalmology, Wayne University College of Medicine, Detroit, Michigan.

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Hospital Insurance Ideals

The American Hospital Association today said it believed individuals would have the best type of hospitalization prepayment coverage "when extensions of coverage for prolonged illness are supplementary to and integrated with adequate coverage of short-term illness."

This statement was part of Recommended Benefits of Prepaid Hospitalization Plans, a guide published in the August 16 issue of *Hospitals, Journal of the American Hospital Association*. The document points out that "there are groups for which it is difficult to make benefits sufficiently inclusive, and certain health services which are not generally available."

The guide urges prepaid health care plans to "encourage the use of outpatient facilities, long-term care facilities, and home care programs when necessary health care can be provided in or through such facilities at less cost than inpatient care in a general or special short-term hospital."

It observes that "While payment for necessary health care is primarily the responsibility of the individual or the family unit, government and the community have a legitimate responsibility to provide or to assist in paying for necessary health care for those people who are unable to finance it themselves."

Necessary health care is defined as "the total diagnostic and treatment services made available through hospitals and related institutions, which are required for the proper care of acute and prolonged illness." The guide says, "Such health care should be made available for as long as the responsible physician may prescribe in accordance with sound medical practice."

Desirable benefits of prepayment for necessary care in general hospitals should include, according to the guide, "the requisite days of care in a multiple bed accommodation and the unrestricted use of the special services provided through the hospital."

A three-day cold costs the average person $25. And, says the Kansas State Board of Health, colds cause 50 to 60 per cent of all absences from work.

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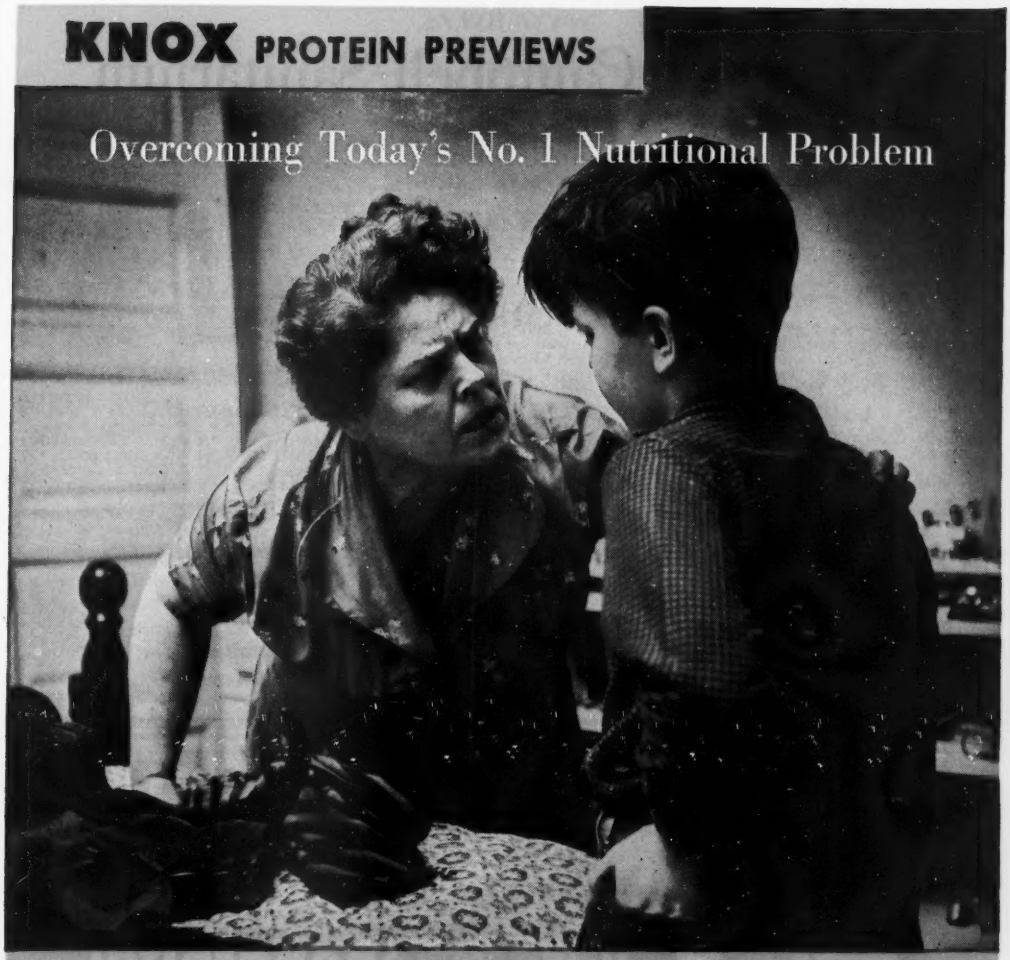

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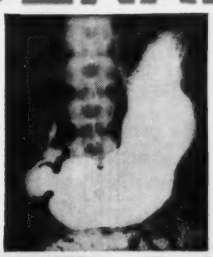

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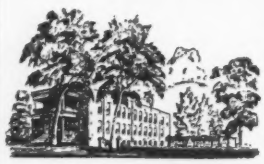

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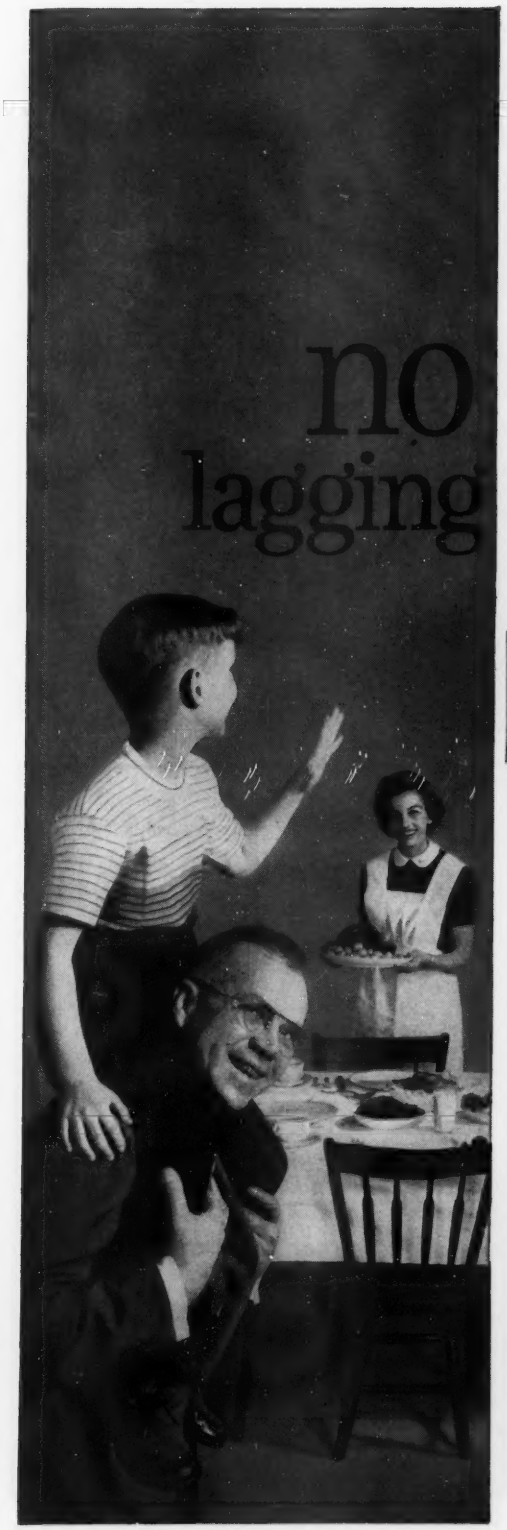

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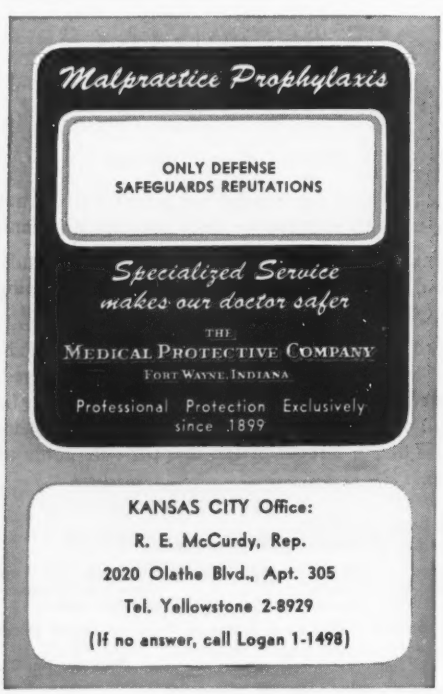
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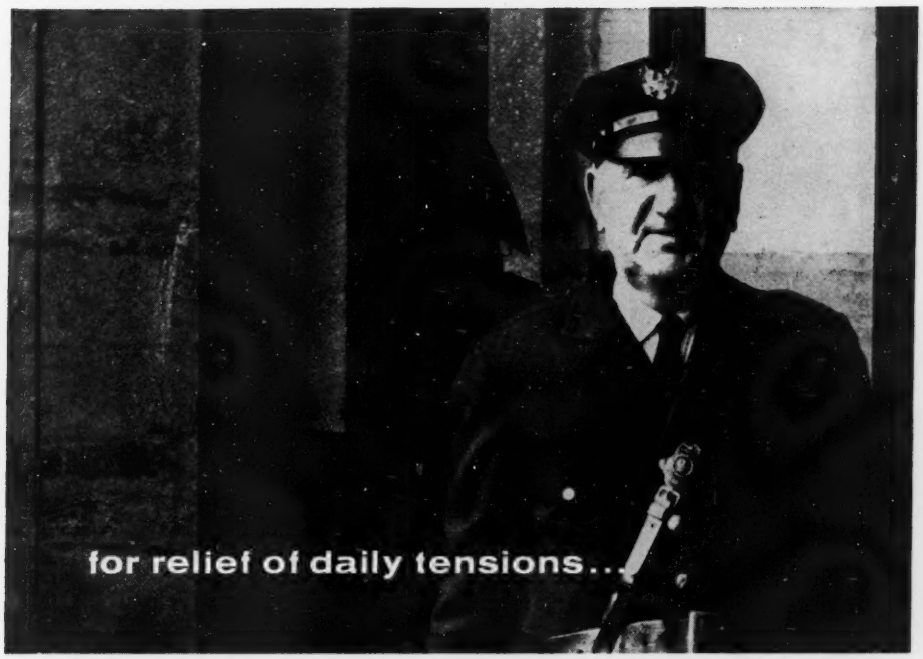

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*Ferguson, J. T., and Linn, F. V. Z.: Antibiotic Med. & Clin. Therapy *3*:329, 1956.

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